

Introduction

The *amount of energy provision in the organism*, that is, primarily the resynthesis of adenosine triphosphate (ATP) according to the needs of the body, is the major factor influencing the health peaks and troughs of human life. This simple biophysical thesis is recognizable as a basic law of our existence when one remembers that the reduction in physical and mental powers, that is, energy deficiency, is a *main characteristic of extreme old age*. Furthermore, in this connection we should remember the *main characteristic of conditions of weakness of all kinds*, which is that in such phases the organism minimizes its energy requirements by lack of movement (e.g. bedrest), in order to ensure the balance between the critically reduced energy provision, and energy consumption. Finally, everyone knows that a high provision of energy is a *main characteristic of youth*. These considerations lead to a way of thinking that is still unusual in present day medicine, a way which may even at first seem disconcerting. But they force us to the conclusion that all events, mechanisms and processes which weaken, strengthen or even lastingly increase the provision of energy in the organism are of fundamental significance for both theoretical and practical medicine in particular for the prevention, prophylaxis and therapy of all diseases, crises or complaints with energy deficiency as their common cause. It follows that the *quantitative determination of energy provision in the human organism* leads to a comprehensive diagnostic characteristic value of exceptional significance.

Even after just the first steps along the way outlined the question of the *bottleneck in energy formation in the organism* appears. It is known that energy is generated in the organism mainly as chemical energy in the form of energy-rich phosphates, particularly as adenosine triphosphate (ATP) [1], discovered in Berlin-Dahlem in 1930 by K.H. Lohmann. Under normal living conditions the *formation of these energy-rich phosphates* is not limited by the intake of food but *by the oxygen transport to the body tissue*. The determination, the natural dynamics, and the process of increase in the O_2 transport to the body tissue become the key to further progress. We recognize that "Oxygen is the giver of life!" The words of Otto Warburg, which were

repeatedly spoken in discussions with him in his Dahlem Institute of Cell Physiology, made a deep impression on the author. This, not only because they came from the researcher who contributed more than any other to the explanation of the respiration and fermentation metabolism of living cells, but because such a comprehensive biological basic truth is contained in this short theorem.

O_2 presents itself as the energetic prerequisite for the differentiation of cells in the slow phylogenetic and the fast ontogenetic development of more highly organized life. O_2 thereby also proves itself to be the prerequisite for the maintenance of life, and its deficiency leads to complaints, suffering, diseases or death.

The generic term " *O_2 deficiency*" can be defined as the combined or individual effect of *critically reduced O_2 transport* to the tissues (O_2 offer to the tissues), *critically reduced O_2 utilization* of the tissue, and *critically increased O_2 requirements* of the tissue.

The long-lasting (e.g. for weeks to months) amelioration or elimination of O_2 deficiency and, moreover, *an increase as strong and as long-lasting as possible in the O_2 transport to the body tissue, is the aim and effect of oxygen multistep therapy (O_2 MT).*

Various procedure variants, some with different fields of indication, are practised. Alongside the 36 h O_2 multistep procedure, which requires more time and energy, a *15 min O_2 multistep quick procedure with simultaneous physical exertion* has been developed, which can free the organism from its deficient situation in just over 30 min. O_2 multistep short procedures have also been designed for nonable-bodied patients. For these patients the increase in cardiac output and in the respiration minute volume is brought about, not by physical exertion, but by drugs. All these procedures generally cause an increase in the arterial resting PO_2 and a drop in the mixed venous resting PO_2 , or an increase in the O_2 absorption and/or CO_2 production at rest, in addition to an increase in the physical performance capacity. Moreover, the improvement which occurs in the O_2 status is reflected in a shortening of reaction times and a drop in the "biological age", an improvement in infor-

mation-psychological capacity and an increase in the host's defense.

All O₂MT variants have in common the fact

that, through the combination of several synergistic steps, the threshold of energy formation is crossed locally in the area of the capillary wall cells, by which the discovered cellular *capillary wall switching mechanism of the microcirculation* is switched in a positive direction.

In all variants of the "oxygen multistep therapy" [2, 3], the method of triggering the switching, i.e. to obtain the long-lasting effect, consists in the combination of the following basic steps:

1st step: *Increase in O₂ utilization* in tissues and cells by means of drugs taken approximately 30 min before start of step 2, e.g. 30 mg vitamin B₁, 75 mg dipyridamol, 100 mg magnesium orotate [4], possibly in the form of the combination preparation "Oxygenabund". For long-term effect the dose is continued once daily for an unlimited time.

2nd step: *Great increase in the O₂ partial pressure in the alveolar space of the lung* during the procedure, by supply of O₂, e.g. using applicators of synthetic material with storage balloon for a long [5] as well as for short duration of procedure [6], with a very high O₂ flow required. When the procedure duration is long, the O₂ flow should be arranged so that the alveolar P_{O₂} is increased from resting normal 100 mmHg (13.3 kPa) to approximately 200 mmHg (26.6 kPa), or so that the arterial P_{O₂} reaches levels close to 125 mmHg (16.7 kPa). For short procedure duration (< 1 h) oxygen-air mixtures are given at 60 to approximately 95 vol.% O₂ using an applicator mask and adapting the O₂/N₂ flow to the patient's respiration minute volume (RMV) [6], which has been greatly increased by exertion.

In special cases (e.g. chronic lung damage, circulatory insufficiency, preshock conditions, emergency situations etc.), when the arterial pO₂ remains too low despite O₂ inhalation, additional immediate aid can be given by means of a simultaneously implemented HOT* procedure [7] (or i.v. administration of

drugs to increase cardiac output), whereby the O₂ transport to the organism is substantially improved.

3rd step: *Increase in blood flow, or at least the*

securing of good circulation in central organs such as heart and lung, or perhaps also of special areas of the organism [8] during the effect time of the 1st and 2nd steps [6]. Increase in cardiac output by physical exertion adapted to the patient's condition [6], or by drugs in nonable-bodied patients. Simultaneous occurrence of the 3rd step with the effect time of the other steps causes intensification, i.e. allows a significant reduction in time and oxygen [6] in the programming of the procedure. In the implementation as part of a cure (36 h O₂ multistep procedure) the physical exertion between the procedure session is planned as daily exercise training [9, 10, 11, 12]. In order to ensure a lasting O₂MT effect the daily exercise training is to be continued daily for an unlimited time. Use of the lastingly increased energetic status for an energetic lifestyle.

The *definition of oxygen multistep therapy* can be considered to be: O₂MT is a repeatable combination of measures for humans, carried out within a defined time-planned sequence, with the aim of a long-lasting increase in the resting O₂ uptake or in the arterial resting P_{O₂} and (or) reduction in the venous resting P_{O₂}. The practical result is an increase in the O₂ transport to the body tissue lasting for weeks to months, with a corresponding rise in the energetic status.

Each of the three steps has an individual, measurable effect and has been part of standard medical practice for a long time. As early as 1798 (!) a book reports on the use of oxygen as a cure [13]. But only when the three steps are connected as given, according to type and time-programming, does the rather surprising, lasting effect occur, i.e., as we know today, the *bioenergetic altering of the course of the discovered cellular vessel wall switching mechanism of the blood microcirculation in a positive direction and in all tissues of the organism*. This effect was hardly likely to be found under clinical conditions (e.g. in intensive care wards) as these, instead of increasing circulation as demanded by the 3rd therapy step, usually strongly reduce it.

In the last few years the time has become ripe for a broader preventative, prophylactic and therapeutic use of O₂ multistep principle. There are several reasons for this:

1. *The exercise-deficient lifestyle* (circulation deficit, drop in arterial PO₂, O₂ deficiency) of people in industrialized countries has increased to a dangerous extent, and is still increasing. Motors have taken over physical labor. Microprocessors of modern electronics and robots increasingly control instruments, installations, machines and production processes of all kinds, without human involvement. Desk work, meetings, time spent travelling or in front of the television occupy an increasing proportion of our daily lives, both at work and in our free time.
2. Thanks to great medical progress in the combat of life-threatening diseases and conditions, *human life expectancy has greatly increased*, and more and more people reach old age, in which cardiopulmonary performance, and, with it, the O₂ supply to the tissues, drop to 50% or less of the levels of youth. It is one of the current tasks of modern medicine to help these people by maintaining their physical and mental performance capacity and to make their lives worth living by the amelioration of the sufferings and complaints of old age.
3. It was not until the last decade that *instruments* were developed in the GDR (in our Institute), and more recently also in the FRG and the USA, which are operated from the electrical network, are easily transportable, and which, *by means of simple processes* (e.g. with zeolites or O₂ selective membrane systems) *enrich the oxygen from the atmospheric air* from approximately 20% to 90%. These new instruments facilitate the provision of inhalation air with an increased O₂ content, independent of heavy pressure cylinders as O₂ stores, and independent of central large installations (e.g. with liquid oxygen). This new type of instrument can make possible in the foreseeable future the provision of O₂ even for households and areas of world health care in which the continuous provision of O₂ has so far caused difficulties.
4. Our discovery that the strength of the host's defense capacity is dependent on the quality of the O₂ status, and is significantly increased by the procedure of oxygen multistep immunostimulation, has opened the way to *bringing the length of one's own life close to the upper age limit of the human organism*.

5. Clinical 5-year results with oxygen multistep immunostimulation have shown that a significant *drop in the probability of metastasis in cancer* can be achieved with the course on which we have embarked, and that when the procedure is repeated once a year, even the concrete, simple solution of a *general cancer prophylaxis* emerges.

The primary target area of O₂ multistep therapy is the lung-heart system. In our investigations into this complex system we have found strong dynamics and reactivity in the co-acting parameters, which are reflected globally in changes in the arterial resting PO₂ (as a resultant). The occurring increase in the alveolar O₂ pressure (increase in the PO₂ of the lung ventilation by means of physical exertion) has a direct, therapeutic effect, particularly on the highly reactive alveolocapillary ventilation, perfusion and diffusion system of the lung. How exciting, then, from this point of view, was the first post-therapy finding of an increase in the arterial resting PO₂ to levels of nearly 100 mmHg or 13.3 kPa (!), lasting approximately 18 months, due to O₂ multistep therapy in a 70-year-old volunteer whose levels 6 years earlier were about 75 mmHg, or 10 kPa.

Particularly strong effects can be expected from the increase in the critically reduced arterial resting PO₂ caused by old age or stressful influences, and from maintaining this characteristic value at a permanently high level (repetition of therapy as stipulated by control measurements), when the pressure gradient for O₂ diffusion to the target area is determined *directly* by the arterial PO₂. That is the case, for example, in the O₂ supply to the eye lens, to the cartilage, the vocal chords and the arterial vessel walls, when physiosclerosis generally leads to noticeable impairment after roughly the 50th year of life. The O₂ metabolism in the walls of the arterial vessels and of their highly-stressed branching points is fed to a large extent directly by O₂ diffusion from the lumen. The great increase in the arterial O₂ partial pressure which occurs *during* therapy, and the drop which usually occurs *after* our therapy, therefore have full effect in these crucial areas. Numerous findings on 50- to 70-year-old hypo- and hypertensive subjects with post-therapy blood pressure levels of around 135/75 mmHg or 18/10 kPa (≅ average levels of 30-year-old volunteers) give an idea of the renormalization of the RR levels (blood pressure measurement according to Riva-Rocci) or of the peripheral vascular resistance attainable through O₂ multistep therapy.

From the view of pathophysiology the new pos-

sibility of increasing more or less permanently the arterial PO_2 in older (and often also in sick) people, and of simultaneously reducing the venous P_{O_2} means the opening up of a *natural*

causal prophylaxis and therapy for the many O_2 deficiency diseases and complaints of old age. It is, after all, a return of the O_2 supply situation as in the best years of youth! In the foreground we can recognize a therapy measure that is permanently effective against arteriosclerosis, and a natural prophylaxis against myocardial infarction — against the main causes of death in our time. A concrete methodology, close to nature, and of great universality is here ready for future preventative medicine.

Various influences and events have temporarily delayed the scientific recognition and assessment of the results of our O_2 multistep therapy research:

1. The long-term duration of an increase in the arteriovenous O_2 saturation difference contradicted the experience and theories of the pulmologists. But is it not precisely the unexpected, the surprising, that is the hallmark of a discovery?
2. As a result of methodological deficiencies which could easily have been avoided by prior consultation with us, the "switching threshold" of the discovered capillary switching mechanism of the blood microcirculation was not crossed in two important institutes and as a result our PO_{2-art} measurement results were not at first confirmed. These findings were unfortunately used as the basis of a series of discriminatory publications and hampering, premature decisions. In one of these institutes our findings on the lasting increase in the arterial PO_2 in volunteers with low starting levels were confirmed in autumn 1982. Our findings concerning the lasting drop in the venous resting PO_2 have not yet been considered.
3. Publication of our results in respected medical journals was repeatedly prevented by conservative, subjectively-judging members of the editorial boards. Such censoring touches a phenomenon discussed worldwide in the pushing through of new scientific knowledge [14].
4. Since the author changed in 1960 from physics to medicine (since then 52 semesters of research study into medicine and physiology), O_2 multistep therapy was downgraded in some quarters as an "outsider method" [15, 16]. It was thereby overlooked that the medical research in our Institute has for many years rested on the basis of an inte-

grated team of doctors, with internists and representatives of the branches of oncology, sports medicine, biology, biochemistry and biomedical engineering, and that a multi-

disciplinary view often brings with it many advantages.

The *basic effect of O_2 multistep procedures* (short definition η^+ -effect), the long lasting increase in the resting O_2 uptake, or of the arteriovenous O_2 saturation difference of the blood, can no longer be seriously doubted. The *basic effect has been statistically proved with a large number of patients* (11 different studies with 2682 volunteers [17]) *and high significance.* Today it is reproduced daily in a good 300 cure institutions and in the process mainly rendered objective by O_2 measurements. Many tens of thousands of patients and volunteers have sensed in themselves the *increase in physical performance brought about by the basic effect*, which we could confirm directly by ergometric measurements [6]. Most recently, the lasting large increase in the O_2 metabolism in the organism after O_2 MT could be directly proven by recording the CO_2 production of the lung (see Appendix).

An accumulation of reports of *good and very good treatment results* [18] can be noted for the indications: renormalization of the O_2 loading of the blood in the lung functionally degenerated by old age or severe stress; early stage of cataract, glaucoma, loss of field of vision, impaired focus; angina pectoris, arrhythmia, prophylaxis and rehabilitation for heart diseases; oedema; peripheral circulation disorders, especially in the lower extremities; circulation disorders, dizziness in old age, senile diabetes; hypotonia, Mb. Ménière; adjuvant therapy in hypertension, general acceleration of rehabilitation; lasting increase in physical performance capacity; defense stimulation, especially after classical cancer treatments, improved quality of life, e.g. in cancer patients.

Individual reports of interesting results, which challenge us to further inquiry, have been received for the following indications: memory weakness, conditions of confusion, side-effects of drugs taken over a long period of time, Parkinson's disease, multiple sclerosis, amelioration of migraine; amelioration of damage to liver and kidneys, amelioration of asthma; rheumatic symptoms complex; acceleration of wound healing.

On the basis of the hitherto amazingly good results, O_2 multistep therapy should prove to be exceptionally effective in the intensification of the host's defense system, and especially in

the implementation of a prophylaxis against cancer metastasis and even of a general cancer prophylaxis [19]. *The combination of the currently usual cancer therapy (operation, chemotherapy, radiation therapy) with an adjuvant triple procedure of O₂ multistep immunostimulation*, discussed in the last section of the book, can be immediately used in the fight against cancer, even in its later stages. The attractive feature of this concept, which is already clinically successful, is that the patient has all the advantages and effects which classical, normal cancer therapy can offer him in his

case. But in addition, he gains amelioration of the side-effects of radiation and chemotherapy as well as, most importantly, often, or with a good probability, the prospect of a halt in the progression of his disease. A broad field for research into such central medical topics, which are decisive for medical practice, presents itself here. When all is said and done it is the improvement in the energy status that is the common key to the medical uses, which have certainly not been fully listed, of the basic effect of oxygen multistep therapy.

1. Physiological foundations

1.1 Basic mechanisms and functions

1.1.1 The discovered cellular capillary wall switching mechanism of the blood microcirculation with varying effects in the lung and other body tissue

1.1.1.1 Ideas on the triggering of the switching mechanism of the blood microcirculation at the venous end of the capillaries

The basic effect of oxygen multistep therapy, the long-lasting increase in the arteriovenous O_2 saturation difference of the blood (η^+ -effect), can, as suggested by numerous signs discussed below, be traced back to *a cellular vessel wall switching mechanism of the blood microcirculation*, which can be triggered by O_2 multistep procedures, and which chiefly starts from the endothelial cells of the capillaries. This switching, or regulating, mechanism is controlled bioenergetically, i.e. *by the energetic status* (hyperoxia and hypoxia) *of the endothelial cells or pericytes of the capillaries, and occurs in all capillaries of the organism simultaneously and concurrently*. It therefore has the fundamental characteristic of a comprehensive effect.

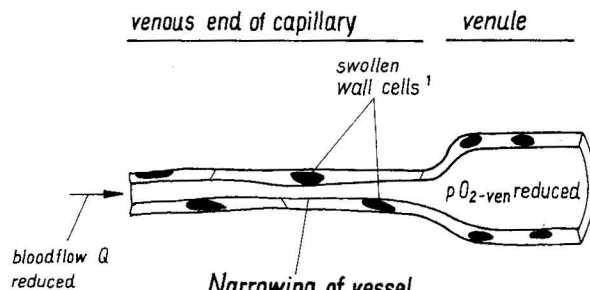
This mechanism is generally (but not always) reversible, i.e. the blood microcirculation can be strengthened by the switching effect (positive switching, η^+ -effect) or weakened by it (negative switching, η^- -effect). We were led to the discovery of this mechanism by the observations already mentioned that it *generally occurs in all capillaries of the human organism. Its effect is different in the lung and in other body tissue*. In the lung the bioenergetic control of the microcirculation leads to changes in the levels of the arterial pO_2 , and in the other body tissues to changes in the venous pO_2 . This mechanism is being discussed at the beginning of this book due to its fundamental significance for oxygen multistep therapy and the research connected to it.

The author obtained, in 1977, the first experimental clue that a reversible switching mechanism of the microcirculation (in the lung) must exist, from the surprising finding that the arterial resting pO_2 , which falls greatly in old age, can by means of an O_2 multistep procedure of a total duration of approximately

36 hours, be raised to levels otherwise generally measured in youth [3]. Further clues resulted from the course of the arterial pO_2 levels measured after severe distress and subsequent combat of the consequences of stress [20]. The decisive clues presented themselves early in 1982 when it was discovered that O_2 multistep procedures also cause a lasting drop in the venous resting pO_2 [6]. In the course of this work, in interaction between literature studies and our own research into the selective staunching of the blood microcirculation in cancer tissues using the cancer multistep therapy measures [22, 23], increasingly concrete *ideas of the cell physiology of the bioenergetic control of the reversible switching mechanism of the microcirculation* were developed.

Stimulated by the intravital microscopic observations of Lübbers and co-workers on the electric triggering of changes in the cross-sections of capillaries, caused by endothelial cells and pericytes [24], as well as by intravital microscopic observations in his own institute, the author came to his ideas on the cell physiology of the switching mechanism of the microcirculation [25] shown roughly and schematically in Fig. 1. It is assumed here that reversible changes in form, and swellings of the vessel wall cells (endothelial cells, pericytes, which are dependent on the degree of their O_2 supply) influence the narrowest inner cross-section of the capillaries. This assumption is in harmony with old experimental findings on the transformation from an elongated to a spherical cell form (epithelial cells) in ATP deficiency [26]. Electron micrographs produced direct pictures of the narrowing of capillaries due to swelling of endothelial cells in energy or O_2 deficiency (hypoxia). The picture in Fig. 2, taken from Loewe and co-workers [27], shows the stage of initial swelling of the endothelial cell. It can be seen

Primary O_2 deficiency causes an O_2 (energy) deficit in the wall cells at the venous capillary end, which then swell and thereby lead to a narrowing of the vessel with reduced bloodflow.



intensifies the above-mentioned O_2 deficiency by:

1. Reduced bloodflow Q
2. Increased apparent blood viscosity

Therefore a system with a switching property (change-over when a threshold level is exceeded). The change-over threshold is determined by the level of the venous pO_2 and its duration of influence as well as by the blood flow intensity.

Fig. 1 Ideas for the triggering of the switching mechanism of the blood microcirculation at the venous end of the capillaries in O_2 deficiency

¹ H_2O flows into the cells as a consequence of the failure of the K^+/Na^+ pump, which requires a great deal of energy

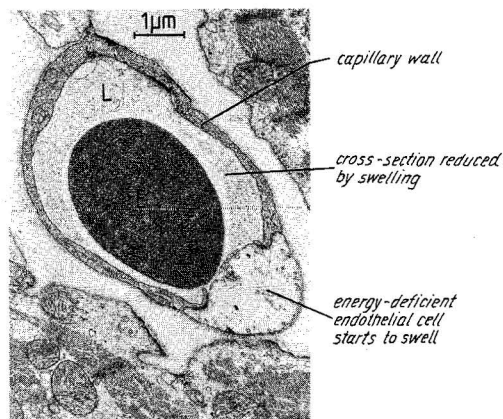


Fig. 2 The elementary process of the switching and regulating mechanism of the blood microcirculation at the venous end of the capillaries in the electronmicroscopic picture. (Loewe et al. [24]. It was discovered that these swellings of the endothelial cells, if not yet at too advanced a stage, can be *lastingly* reduced by O_2 MT procedures. Blood microcirculation strengthened in all perfused capillaries of the organism, weakened in distress. L = capillary lumen; E = erythrocyte

from further photographs and measurements that there is always a transition to total occlusion by the swelling of the capillary endothelium. We could derive from PO_2 measurements that, up to a certain intermediate stage, the switching mechanism remains reversible, and this is the area of influence of the O_2 multistep procedures. Here it should be noted that, according to the PO_2 course between the arterial and venous ends of a capillary shown in Fig. 3, the bioenergetic control of the narrowest capillary cross-section is to be expected primarily near the venous end of the capillary, because

the lowest PO_2 levels are to be found there. A high proportion of the cell energy serves the maintenance of the sodium pump (Na^+/K^+ -ATPase, osmoregulation of the cell). In energy deficiency in the wall cells at the venous capillary end, a reduction in the pump performance occurs and, with it, an accumulation of hydrated sodium ions [28]. The swelling which then occurs can be removed by the restoration of a good energy situation (high PO_{2-ven}). Further details of the pathophysiology of the endothelial cells can be found in [29, 30] and in the literature references 4 to 6 in [27].

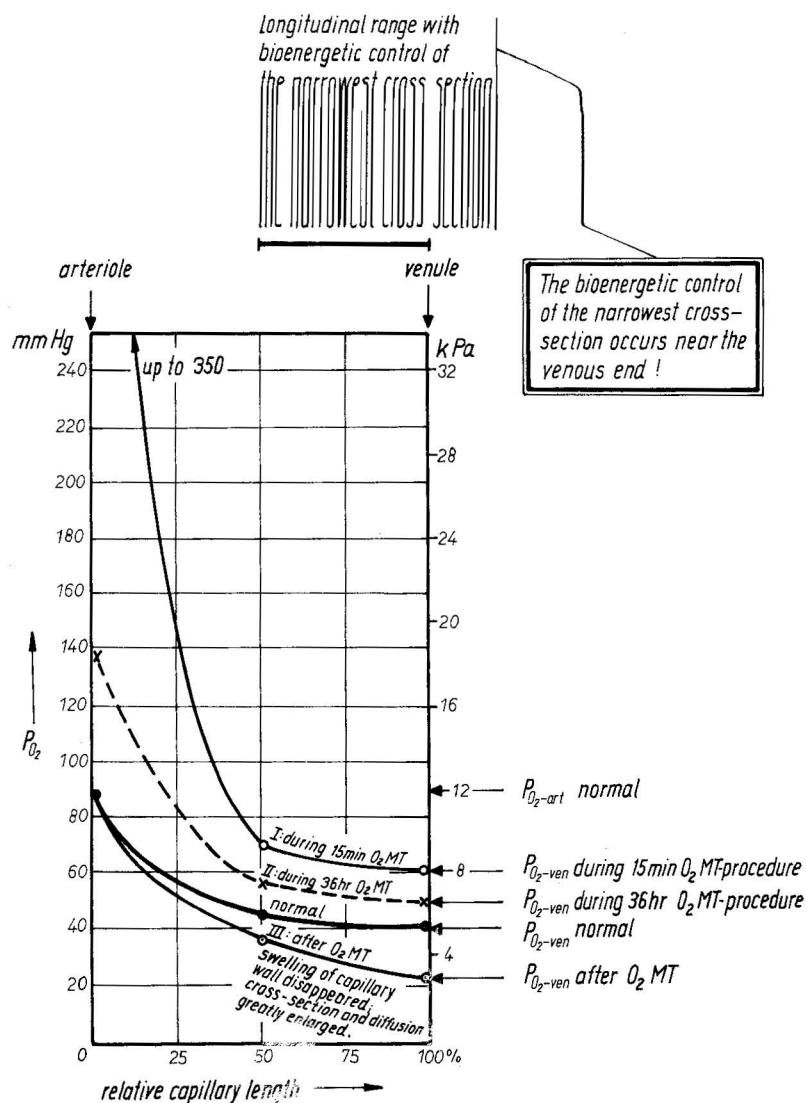


Fig. 3 Example of PO_2 courses between the arterial and venous ends of a capillary during a 15 min O_2 MT procedure (II), and after O_2 MT (III). The values of PO_{2-ven} increase with PO_{2-art} and blood flow in the envisaged capillary under O_2 application of O_2 MT treatment

In order to explain the long-lasting effect, i.e. to justify the interpretation that we are dealing with a real switching process, it is necessary to show that, in the bioenergetic control of the narrowest capillary cross-section, it is a *system with feedback*. This can be immediately recognized when we remember, for example, that the primarily poor O_2 supply situation leads, via the triggered narrowing of the cross-section with a drop in the blood microcirculation, to a further significant deterioration in the O_2 supply. The deterioration is even further intensified because the apparent blood viscosity increases as a result of a reduction in the shear stress in the blood flow, as in Fig. 4. This chain of deteriorations in the O_2 supply signifies the *existence of a system with positive feedback*.

Such systems have, as is generally known, the property of bringing about a change in quality by an accumulation of quantitative elements. They have *switching properties* when a certain degree of feedback is crossed. Beneath this switching threshold there is only a control with a greater or lesser enhancement effect, but this is not of any duration. It can thus be understood that, in the implementation of the O_2 multistep procedure, a certain threshold of the oxygen dosage applied must be crossed, in order to maintain the high η^+ -effect for a long period of time. In Table 1 there is a compilation of the characteristics of the bioenergetic control dose for the "switching" or "regulating" areas, and the procedure variants discussed below. The same distinction also applies

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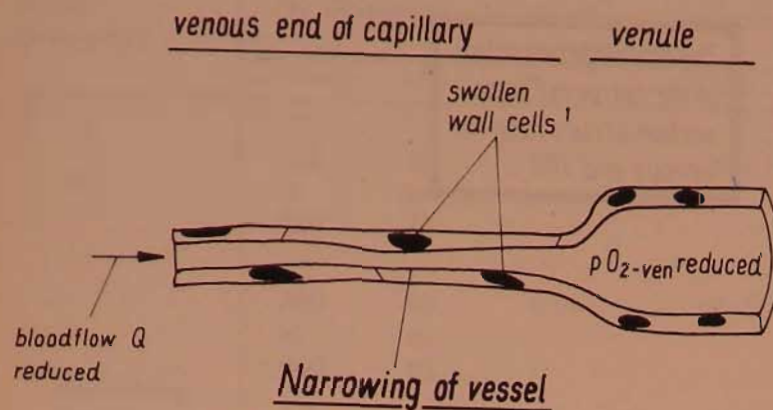
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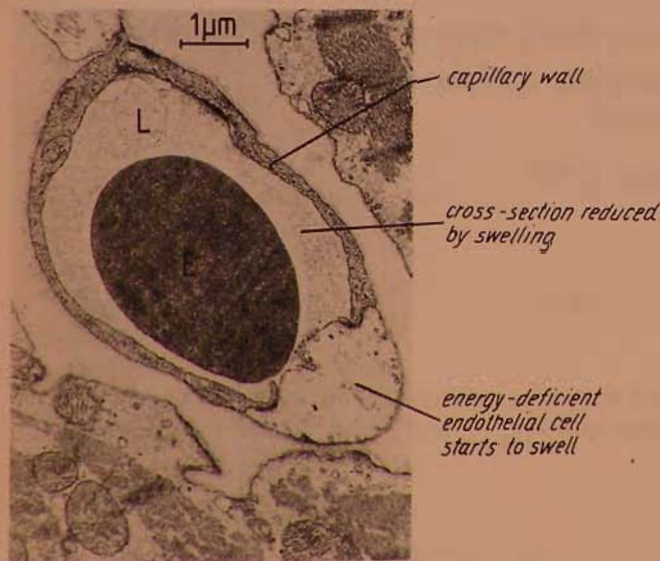


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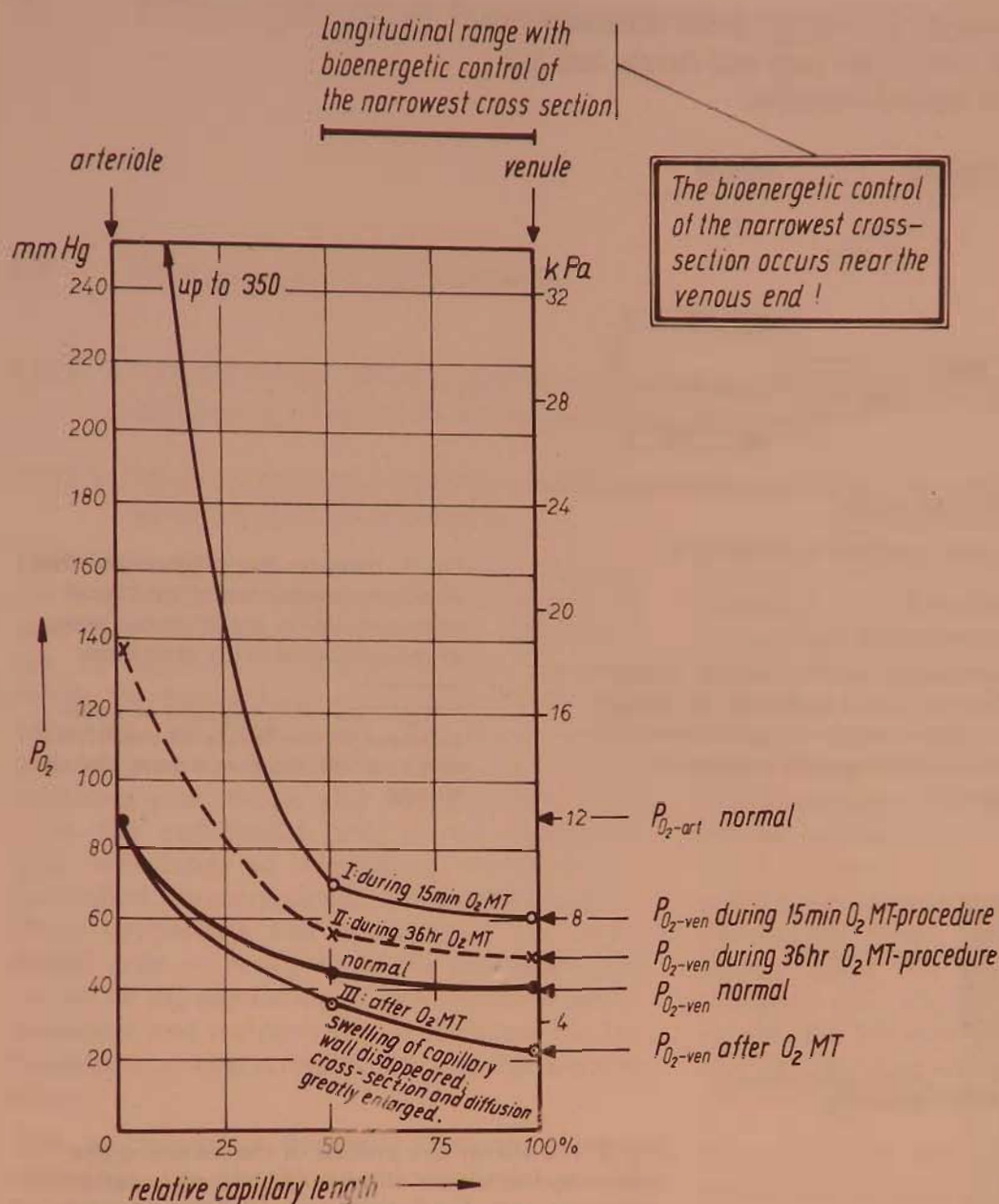


Fig. 3 Example of P_{O_2} courses between the arterial and venous ends of a capillary during a 15 min O_2 MT procedure (II), and after O_2 MT (III). The values of P_{O_2-ven} increase with P_{O_2-art} and blood flow in the envisaged capillary under O_2 application of O_2 MT treatment

In order to explain the long-lasting effect, i.e. to justify the interpretation that we are dealing with a real switching process, it is necessary to show that, in the bioenergetic control of the narrowest capillary cross-section, it is a *system with feedback*. This can be immediately recognized when we remember, for example, that the primarily poor O_2 supply situation leads, via the triggered narrowing of the cross-section with a drop in the blood microcirculation, to a further significant deterioration in the O_2 supply. The deterioration is even further intensified because the apparent blood viscosity increases as a result of a reduction in the shear stress in the blood flow, as in Fig. 4. This chain of deteriorations in the O_2 supply signifies the *existence of a system with positive feedback*.

Such systems have, as is generally known, the property of bringing about a change in quality by an accumulation of quantitative elements. They have *switching properties* when a certain degree of feedback is crossed. Beneath this switching threshold there is only a control with a greater or lesser enhancement effect, but this is not of any duration. It can thus be understood that, in the implementation of the O_2 multistep procedure, a certain threshold of the oxygen dosage applied must be crossed, in order to maintain the high η^+ -effect for a long period of time. In Table 1 there is a compilation of the characteristics of the bioenergetic control dose for the "switching" or "regulating" areas, and the procedure variants discussed below. The same distinction also applies

Table 1 Typical threshold levels for switching or regulating blood microcirculation through variants of O₂ multistep therapy

Bioenergetic control of micro-circulation	Characteristics of the threshold levels					Type of process
	$P_{O_2\text{-art}}$ with O ₂ inhalation		duration of process	cardiac output	Adjuvant steps	
	mmHg	kPa	h	l/min	no. of repetitions	
1 Switching (lasting η -effect)	1.1 120 to 150	16 to 20	36	5 to 6	0	36 h O ₂ multistep procedure
	1.2 300 to 400	40 to 53	0.25	10 to 16	1 to 2	15 min O ₂ multi-step quick procedure
	1.3 120 to 150	16 to 20	36 to 0.75	5 to 6 to 10 to 16	0 (3)	combination of 36 h procedure + 15 min quick procedure
	1.4 120 to 150	16 to 20	36	5 to 6	0 e.g. 8 x HOT*	combination of 36 h procedure + HOT* (simultaneity of O ₂ inhalation and HOT*)
	Threshold!	no O ₂ applied	≈ 36	≈ 16	0	Stamina training over several weeks
2 Regulating (no lasting η -effect)	2.1 < 100	< 13	36	5 to 6	0	36 h O ₂ M procedure (when $P_{O_2\text{-art}}$ under O ₂ inhalation too low)
	2.2 120 to 150	16 to 20	< 18	5 to 6	0	36 h O ₂ M procedure (when duration of procedure too short)
	2.3		0.25	5 to 6	e.g. 2 x HOT*	HOT* procedure alone (often lasting effect)
	2.4 [— —]		some h	10 to 16 (50 to 100 W strain)	—	Exercise training (effect of training lasts about 2 days)
	2.5 e.g. 90 without HOT*, 120 to 150 with HOT*		1	4 to 5	0 immediate $P_{O_2\text{-art}}$ in non-able-bodied patients	simultaneous combination of elevation of O ₂ dose 5 to 10 l/min + HOT* (emergency procedure)
no effect on $P_{O_2\text{-art}}$	3.1 < 80	< 11	36	5 to 6	0	36 h O ₂ M procedure (in cases of severe lung insufficiency)

in reverse for the reduction in microcirculation due to O₂ deficiency, e.g. as a result of stressful influences. Thus the theory of control systems assumes today that, in the case of a myocardial

infarction, a high degree of feedback leads to a switching process with a permanent effect, whereas in angina pectoris a weak degree of feedback keeps the process reversible.

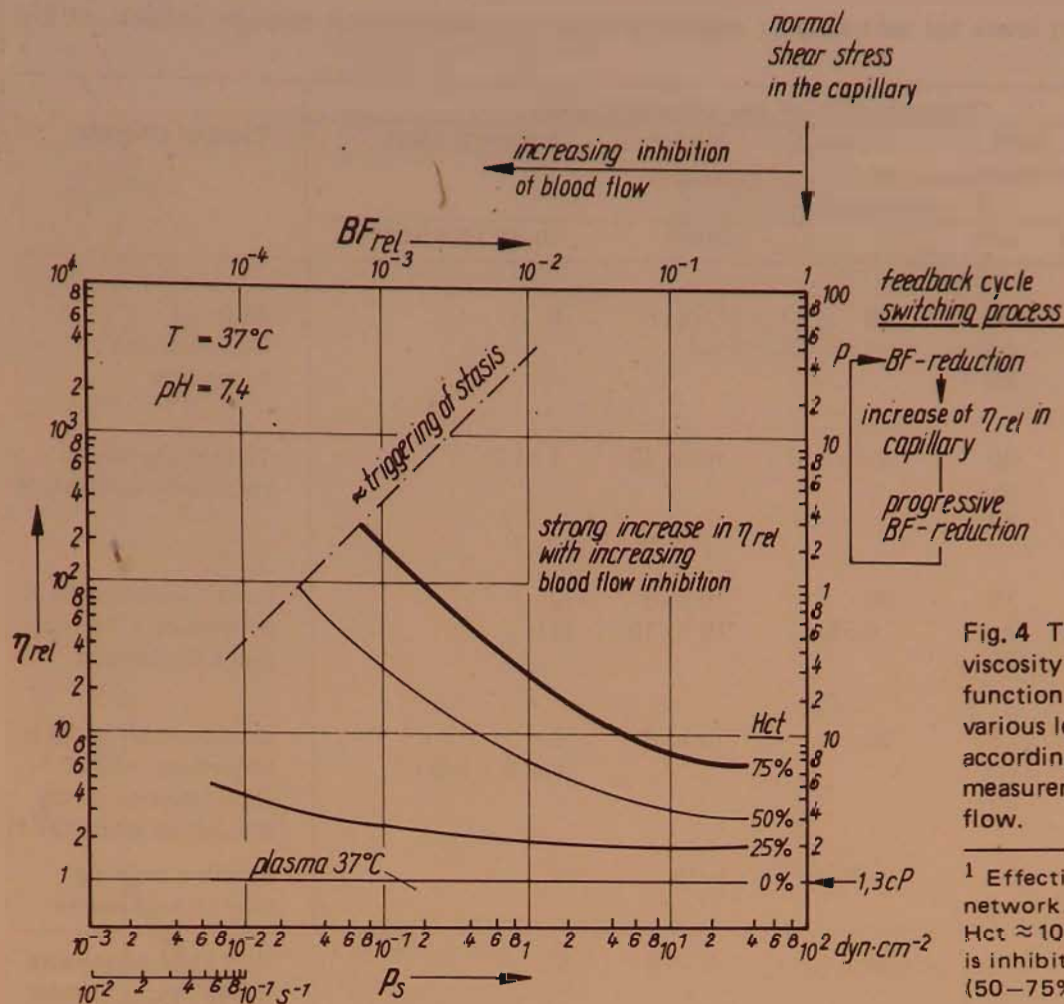


Fig. 4 The relative apparent blood viscosity η_{rel} in larger vessels as a function of the shear stress p_s for various levels of the hematocrit Hct according to Schmid-Schönbein's measurements [31]. BF = blood flow.

¹ Effective hematocrits in terminal network. Normal conditions: Hct $\approx 10\%$. When microcirculation is inhibited, Hct becomes very high (50–75%)

1.1.1.2 Differences in the triggering of the switching mechanism in the various organs and tissues. Relationship to the degree of effectiveness of the O_2 multistep therapy procedures

Differences in the consequences of O_2 deficiency condition in various organs and tissues of the human body on the one hand, and the observed differences in the response for the elimination of O_2 deficiency on the other, stimulated us to investigate the (common) cause for these differences. The cause was thought to lie in a *varying level of the switching threshold of the bioenergetically controlled switching mechanism of the blood microcirculation*. The effect of this mechanism, which occurs generally in the whole body, simultaneously and equidirectionally, is superimposed onto the local regulation processes of the microcirculation, e.g. through precapillary sphincters [32], which have been known and thoroughly investigated for a long time.

At the venous end of the capillaries, where the lowest P_{O_2} level exists, the endothelial cells of the capillary wall begin to swell due to water absorption in O_2 deficiency, because the K^+/Na^+ pump, which demands roughly 30% of cell energy, diminishes in its performance [34]. The swelling leads to the cross-sectional narrowing

already discussed and, after the switching threshold is crossed, to the triggering of the switching mechanism.

The swelling of the endothelial cells in O_2 deficiency is at first of a *reversible nature*, which means that the detumescence of the wall cells and, with it, a renormalization of the reduced blood microcirculation can be achieved by the production of high P_{O_2} levels at the venous capillary end (and of an increased capillary blood flow, e.g. by means of physical exertion) over a certain length of time (detumescence time). The further research into the parameters governing these dynamics is one of the most interesting tasks of the field of microcirculation, as the *switching and regulating mechanism* described seems to be representative for the uniform initial process in myocardial infarction, in shock, in peripheral circulatory disorders, in damage caused by distress etc., as well as, in the opposite direction (which greatly upgrades the microcirculation) in sports stamina training, and in the procedure variants of oxygen multistep therapy.

The duration time for the high-charging of a downgraded microcirculation (detumescence time) is determined by the therapeutically applied PO_2 level at the venous capillary end. The O_2 supply of the endothelial cells at the capillary end by means of diffusion is dependent on this. From the measurements of this in Fig. 3 (guiding values) it emerges that, with the procedure variant with increase in cardiac output by means of severe physical exertion and $PO_{2-ven} = 60$ mmHg (8 kPa) the threshold for high-charging will be crossed with sufficient certainty in 15 min; with the procedure variant without increase in cardiac output, and $PO_{2-ven} = 45-50$ mmHg (6-6.6 kPa) in approximately 36 h.

The aforementioned PO_{2-ven} levels are attained using the standard 15 min O_2 multistep quick procedure discussed below, and the standard 36 h/18 day O_2 multistep procedure.

From the theory of diffusion and from experimental experiences there results the following relationship for the effectiveness W of O_2 multistep therapy procedures and of procedures of hyperbaric O_2 multistep therapy:

$$W \sim (PO_{2-ven \text{ procedure}} - PO_{2-ven \text{ before}})^n \cdot t_{\text{procedure}}$$

Key:

$PO_{2-ven \text{ procedure}}$ = venous PO_2 , measured during procedure with O_2 application. This value is dependent on the arterial PO_2 during the procedure and the bloodflow Q in the capillaries. The Q -level is roughly proportional to the cardiac output and therefore approximately twice as high during the 15 min procedure as in the 36 h procedure. The strength of the microcirculation therefore has a significant influence on the triggering of the switching mechanism.¹

$PO_{2-ven \text{ before}}$ = venous PO_2 , measured before procedure

n = efficiency exponent ≈ 3.5 ; empirically obtained from

the measured values in Fig. 3² and the relationship of the duration of procedures

$t_{\text{procedure}}$ = total duration of the O_2 MT procedure

If, due to the named procedure variants or due to their reversal in the direction of " O_2 deficiency conditions over a certain length of time", the oxygen partial pressure simultaneously changes at the venous end of all capillaries of the organism over a certain time span, a comprehensive effect occurs. It can be measured absolutely by spirometry as a change in the resting O_2 uptake or CO_2 production of the organism. Relative values of this change can be gained from changes in the arterial and venous resting PO_2 (see Section 1.1.5).

In the framework of the application of the O_2 MT it is usually only the total effect that is considered in the judgement of the O_2 situation and its dynamics. A more detailed evaluation was made in [35].

It is known that the O_2 utilization varies greatly, dependent on the rate of O_2 consumption in the individual organs and tissues. This has as a result that the venous PO_2 of the various organs and tissues shows great differences. The scale of PO_{2-ven} levels for normal young persons, resting, is given in Fig. 5 B, bottom row. It reaches 22 mmHg (heart) to 68 mmHg (spleen). The mixed blood carried to the lung has a resting PO_{2-ven} level of 40 mmHg, with physical rest and compensated cardiac output.

It is known that the mixed PO_{2-ven} at rest decreases to roughly 35 mmHg in old age [35]. The reduction is obviously a counter-regulation of nature, to counter the severe drop of the arterial resting PO_2 in old age [37]. Corresponding to the reduction of the mixed PO_{2-ven} of an average 5 mmHg at an age of 75 years, roughly the same reduction of the resting PO_{2-ven} levels assigned to the organs and tissues occurs. The scale of the expected resting PO_{2-ven} levels for older, untreated persons is given in Fig. 5 B, top row.

The O_2 supply to the endothelial cells at the venous capillary end depends on the level of the venous O_2 partial pressure. A high PO_{2-ven} results when a high arterial O_2 partial pressure is

¹ The effect contribution of the optional adjuvant steps of HOT* and hemodilution is mainly reflected in an increase of blood flow Q .

² $PO_{2-ven \text{ procedure}} = 45$ mmHg assumed for the 36 h procedure

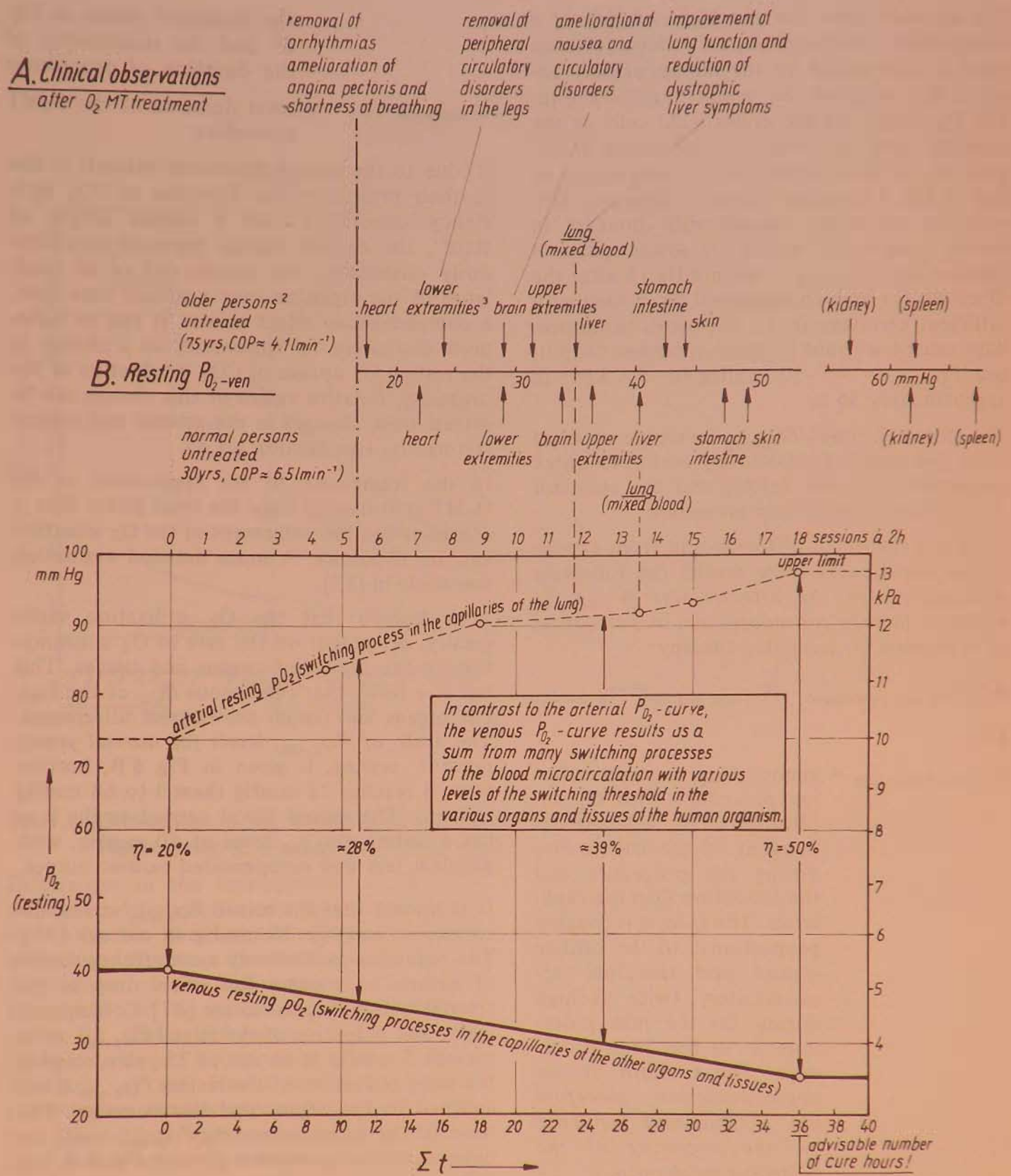


Fig. 5 The correlation between the occurrence of certain clinical observations dependent on the increasing number of sessions of the 36h- O_2 M procedure (A) in various body tissues, and the level of the venous resting P_{O_2} (B) of these body tissues. Below: typical courses of the arterial and venous resting P_{O_2} with increasing number Σt of treatment hours. Volunteers of both sexes, $N = 8$, age 65–85 years. Time of measurements ≈ 10 a.m. During the 1st session the $P_{O_{2-art}}$ was $142 \pm 12 \text{ mmHg}$ under the application of oxygen at a rate of 4 l min^{-1}

¹ Measurement at rest, and standing

² When the $P_{O_{2-art}}$ is lowered (old age, distress), a counter-regulation causes the levels of the resting $P_{O_{2-ven}}$ to drop, the same applies after strengthening of the blood microcirculation by means of O_2 MT. The reduction in the cardiac output COP in old age (reduced blood flow) lowers the threshold for strengthening and weakening of the microcirculation

produced (O_2 MT procedure with high O_2 offer to the lung, adapted to the respiration minute volume RMV) and when there is a high capillary blood flow Q (high cardiac output, physical exertion). The strength of the blood microcirculation therefore plays a significant role in the *triggering of the switching mechanism of the microcirculation*. The reason why a reduction of the microcirculation (cardiac infarction, intermittent claudication) occurs more frequently in older persons may be considered to lie particularly in the decrease in the nutritive capillary blood flow (reduction of cardiac output with age [37]) and thereby in the PO_{2-ven} .

According to these explanations, the scale of the resting PO_2 of the various organs and tissues (Fig. 5 B) gives us a clue to the *mean risk for the various organs and tissues in O_2 deficiency* (old age [37], stressful influences [20, 21]. According to this compromise of the heart (myocardial infarction) could first be expected in O_2 deficiency, due to diminishing of the microcirculation, and then in the lower extremities, and also in the brain (circulatory disorders, dizziness) and in the eyes. Correspondingly it is to be expected that an *improvement of the O_2 status with procedure variants of the oxygen multistep therapy or stamina training*, will help first the heart, then the lower extremities, as well as the brain (circulatory disorders) and the eyes. The above formulated rules give us new insights into the multifactorial process in various important diseases, suffering and complaints based on O_2 deficiency.

Due to the discovered correlation between the quality of the O_2 status and the strength of the host's cellular defense capacity [18], *significant local differences in the strength of the defense capacity dependent on location*, can be expected in the human organism from this viewpoint. This assessment carries more weight when we begin to take into account the local variations in the defense cell density (differences in the parameters of the capillary network and the microcirculation etc.). Cancer tumors can be expected to manifest themselves more frequently in parts of the organism where local minima in the O_2 status and in the defense cell density have existed over a certain period of time. It is particularly easy to recognize O_2 status minima in the area of the skin, e.g. by means of transcutaneous large area measurement of the PO_2 . Skin abnormalities often form the grounds of such minima, which can be made to disappear or at least to weaken by oxygen multistep stimulation of the host's

defense. Investigations of this type lead to an interesting dermatological research area.

The peripheral circulatory disorders in the lower extremities, caused by a deterioration in the O_2 status and often ending in the necessity of a leg amputation, are among the commonest illnesses of old age. This fact can be explained by the low level of the resting PO_{2-ven} measured in a standing position, of this area of the skeletal musculature, already discussed (see also Fig. 5 B), combined with the drop in the resting O_2 uptake of the organism, or of the cardiac output, to a level at the age of 75 years of 65 % or 62 %, relative to the maximum (30 years).

In order to round off our ideas, it seemed necessary to find an answer to the question of why this disease affects primarily the lower, and not the upper, extremities, and why O_2 multistep therapy (and also HOT-UVR therapy) usually gives unique aid particularly in circulatory disorders of the lower extremities (Fig. 5 A). In order to answer these questions, *measurements of the resting PO_{2-ven} at the upper and lower extremities* were undertaken, in a standing position, the mean levels of which can be found in Fig. 5 B. As our ideas had led us to expect, it was found that the *venous resting PO_2 in the lower extremity is significantly lower than in the upper* (measurement in a standing position), by 7 mmHg/0.93 kPa. This result explains the preference of the lower extremities in the pathogenic decharging of the microcirculation in the skeletal musculature, and in the therapeutic high-charging.

Within the framework of these investigations we gained information about the course of the venous resting PO_2 and the blood microcirculation in the lower extremities during the pathogenic and therapeutic processes, summarized in Fig. 6. It may seem disconcerting at first that a poor O_2 supply to the capillary wall cells can exist with a high level of the local mixed PO_{2-ven} (Fig. 6 C) and conversely, that the best O_2 supply (Fig. 6 E) can occur with a particularly low level of the local mixed PO_{2-ven} . These paradoxical findings can be explained by a change in the diffusion areas as a function of the nutritive blood flow Q , which is very low in the first case and very high in the second (see also the above relationship of the effectiveness of O_2 MT procedures). The dynamics of the microcirculation also contribute to the fact that, in the PO_{2-ven} control of the discovered switching mechanism, the PO_{2-ven} levels of the switching threshold for the lowering or raising of the microcirculation are very far apart (Fig. 6, right).

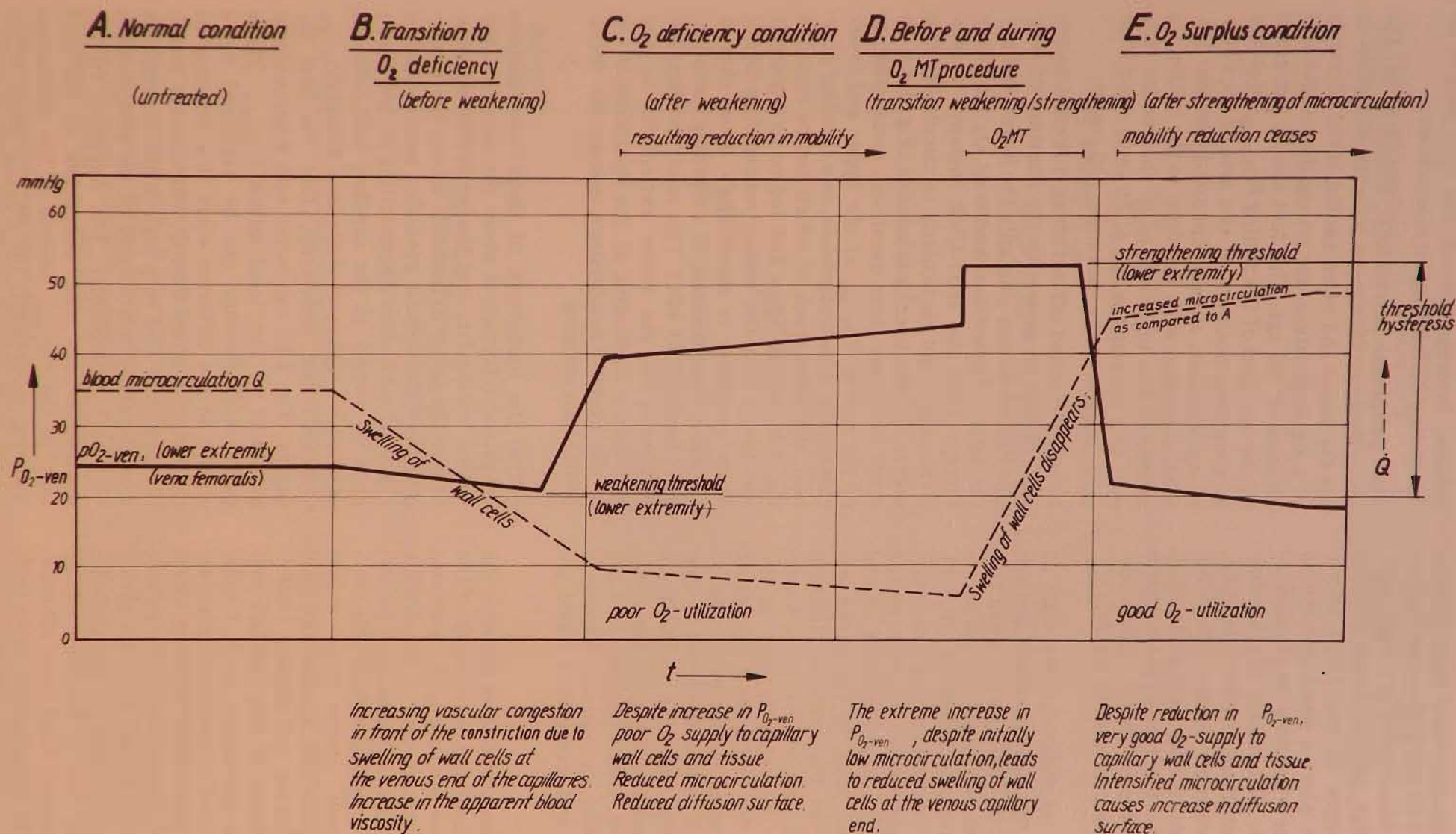


Fig. 6 The course of the venous O_2 partial pressure P_{O_2-ven} and of the blood microcirculation Q in a particular body tissue in the transition from the normal condition (A) to O_2 deficiency (B) and the O_2 deficient condition (C), as well as during (D) and after (E) the reversion of the detrimental state by O_2 MT, exemplified by a lower extremity. Guiding values and speculative ideas

The *physical handicap* occurring due to peripheral circulatory disorders usually leads to a lifestyle lacking in exercise. According to [20, 21] *long term physical inactivity is one of the stressful influences causing a particularly severe deterioration of the O_2 status*. The resultant lack of exercise therefore has as a consequence an intensification of the O_2 deficiency which triggers the reduction of the microcirculation. This vicious circle causes a *particularly stabile consolidation of this detrimental state*: the nutritive capillary perfusion succumbs almost completely. For this reason an *intensive variant of the oxygen multistep therapy* is usually used to combat peripheral circulatory disorders in the lower extremities, in which the standard O_2 MT procedure is combined with a HOT-UVR treatment, which favors the switching process. This intensive variant has already been used against circulatory disorders of the lower extremities in many cases in the now more than

300 centres for oxygen multistep therapy treatment. Numerous successful treatment results have been gained: patients who had for years burdened those around them as severe nursing cases, left their beds and returned to a life with physical exertion; after the O_2 MT, the reduced temperature of the leg was frequently raised to a normal level, and an already planned amputation could be avoided; in almost all treatments in the early stages of this disease there resulted an extremely impressive increase in pain-free walking distances.

We have selected this particular problem and its combat by means of O_2 MT procedures as a classic example, with the intention of presenting a pathogenic process which has the *specific characteristic that it causes an additional deterioration of the O_2 status of the organism, due to the lack of movement caused by the problem itself*.

1.1.2 The O_2 partial pressure and the proportion physically dissolved in the blood during and after O_2 multistep therapy

The bioenergetic control of the switching mechanism of the microcirculation, already mentioned, occurs due to the proportion of oxygen physically dissolved in the blood. Although this proportion is very small, compared with the proportion chemically bound to the hemoglobin, it alone is able to react and is therefore effective. The physically dissolved oxygen is kept at an even level by means of immediate transport from the O_2 fraction chemically bound to the hemoglobin. The *volume of the physically dissolved O_2 fraction in the blood as a function of the oxygen partial pressure* can be taken from Fig. 7. The pressure areas for the arterial and venous PO_2 , existing during and after O_2 MT multistep therapy procedures, can also be found there. The measured temporary increase in the PO_2 levels near the venous end of the capillary (see also Fig. 3) during the O_2 multistep therapy procedures is decisive for the triggering of the switching mechanism of the microcirculation. This *temporary large increase in the PO_2 at the venous end of the capillary* naturally particularly benefits the endothelial cells which are located there and are decisive for our procedure. The increase in the PO_2 at the venous capillary end is favoured when the circulation of the lung and heart is simultaneously significantly increased by means of physical exertion, as in the 15 min

O_2 multistep quick procedure. In the 36 h O_2 multistep procedure an increase is achieved in the PO_2 at the venous capillary end just sufficient for the triggering of the switching process, when $PO_{2-art} > 125$ mmHg (16.6 kPa) is measured under O_2 inhalation.

The increases in the arterial PO_2 during the O_2 multistep procedures (see Fig. 7) only lead to a directly proportional increase in the O_2 diffusion into the tissue in a few areas of the organism. In these few areas, where the course of saturation in the upper part of the O_2 binding curve of the blood does not limit the effects, particularly strong effects of O_2 multistep therapy can be expected and also observed. The *functional elements of lung bordering the alveolar space* can be named here; also *the vessel walls of the arterioles or arteries*, which receive their oxygen, not through the vasa vasorum, but solely, or to a large extent, through diffusion from the relatively large vessel volume. Further examples of this type are the lens of the eye, the cartilage and the vocal chords. Almost all other tissues of the organism receive oxygen via capillaries, the O_2 transport function of the hemoglobin, discussed in the following section, thereby gaining decisive significance.

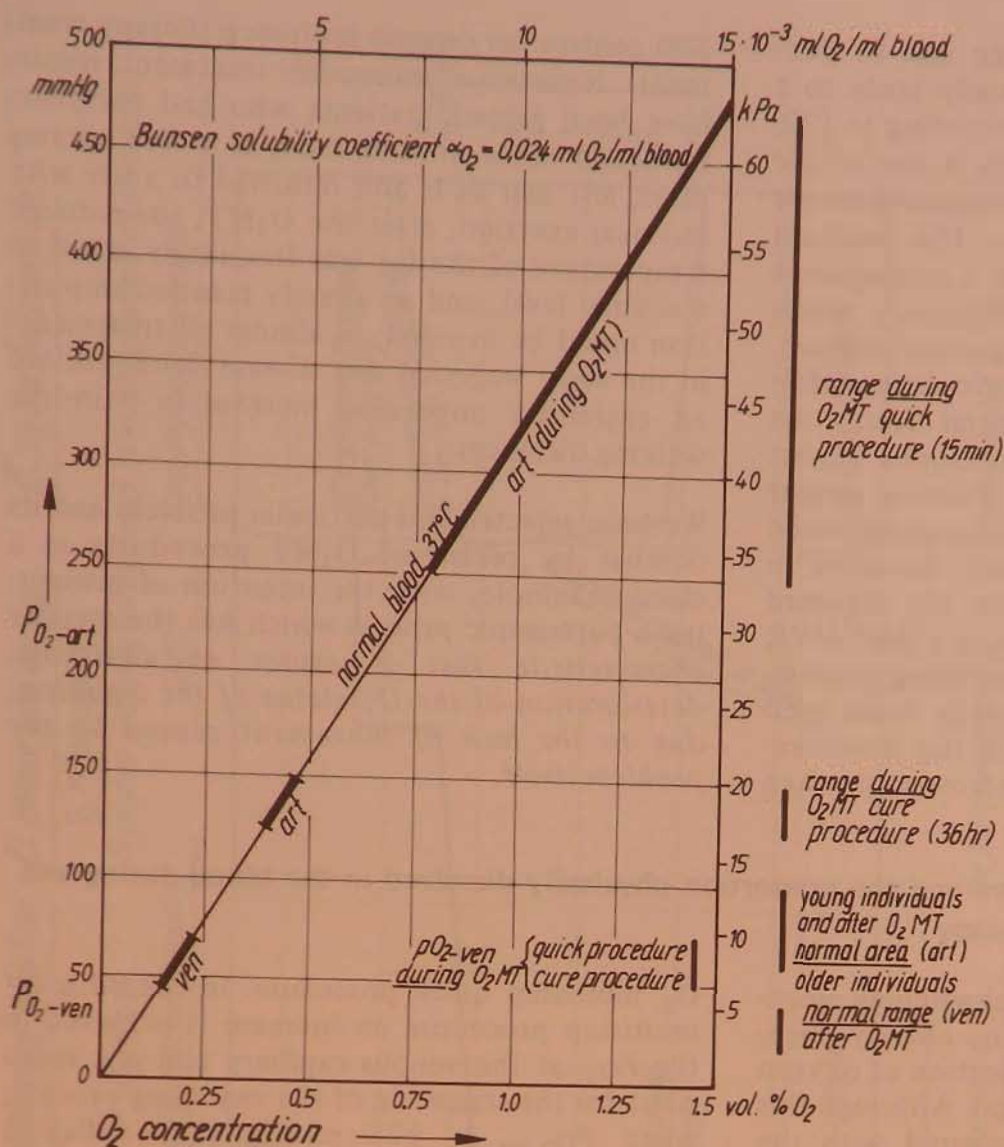
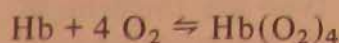


Fig. 7 The physically dissolved O_2 fraction in the blood as a function of the arterial (venous) oxygen partial pressure

1.1.3 O_2 binding curves and exhaustion of the O_2 binding capacity of the blood

Although only very small amounts of O_2 are dissolved in the blood, the physically dissolved proportion is — as emphasized above — of decisive significance for the biological effect and thereby also for the O_2MT , as only the dissolved O_2 molecules can reach their reactants and thus undergo chemical binding.

By far the greatest proportion of the oxygen transported with the blood is *chemically bound to the hemoglobin of the red blood cells* [33]. The reaction of the oxygen with the hemoglobin



follows the law of mass action. It is therefore the physically dissolved O_2 , which, according to Henry's and Dalton's laws, is proportional to the P_{O_2} level, and determines the proportion of the hemoglobin to be transformed into oxyhemoglobin. The proportion of the oxyhemoglobin in the total hemoglobin concentration is termed the O_2 saturation of the hemoglobin:

$$SO_2 = \frac{[Hb O_2]}{[Hb] + [Hb O_2]}$$

This connection between the O_2 partial pressure and the O_2 saturation of the hemoglobin is expressed by the O_2 binding curve of the blood. As Fig. 8 shows, this curve is S-shaped, the steepness being dependent on various parameters (temperature, pH, PCO_2). Fig. 9 gives information about the characteristic of the O_2 binding curve (P_{O_2} range) between O_2 absorption in the lung and O_2 delivery to the tissue in humans (normal and resting conditions). If, as in accordance with this figure, a mean arterial $P_{O_2} = 95 \text{ mmHg}$ ($SO_2 = 97\%$) and a mean venous $P_{O_2} = 40 \text{ mmHg}$ ($SO_2 = 73\%$) are assumed, the content of chemically bound oxygen in the arterial and venous blood can be calculated at about 20 and 15 vol.%, respectively. The arteriovenous difference of the O_2 concentration is therefore 5 vol.%. So normally only approximately of one quarter of the total O_2 binding capacity of the blood is exploited

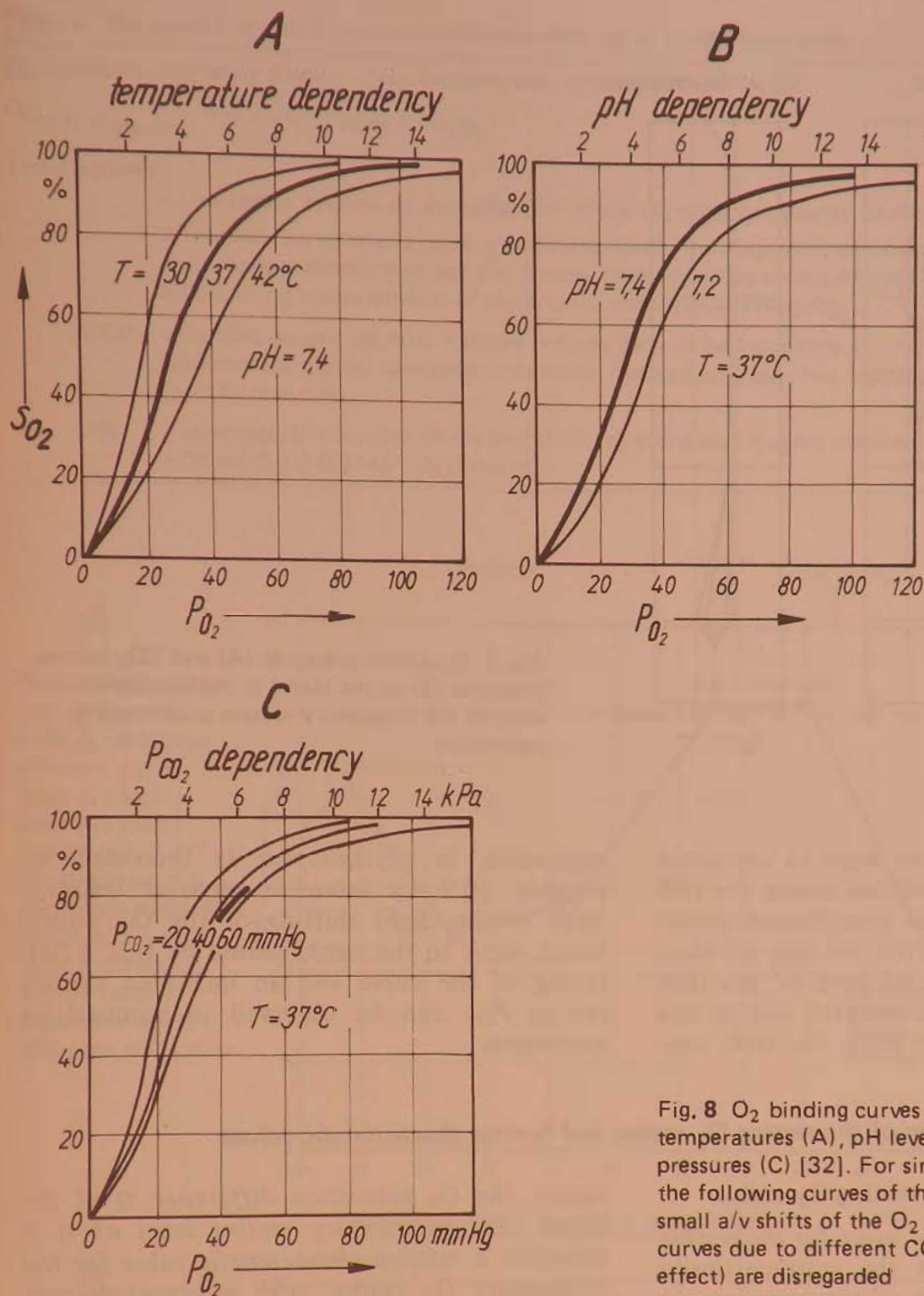


Fig. 8 O_2 binding curves of the blood at various temperatures (A), pH levels (B), and CO_2 partial pressures (C) [32]. For simplification, here and in the following curves of this type in the book the small a/v shifts of the O_2 binding (dissociation) curves due to different CO_2 contents (Bohr's effect) are disregarded

in the circulation through the tissue capillaries. The degree of exploitation of the blood in the

individual organs, according to Fig. 9 and section 1.1.2, varies greatly.

1.1.4 Increase in the O_2 delivery to the tissue by means of artificial reduction of the O_2 affinity of hemoglobin

One method of significantly improving the arteriovenous exploitation of the O_2 binding capacity of the hemoglobin is the artificial reduction of the O_2 binding capacity of the hemoglobin in the red blood cells, for approximately 60 days. In addition to other substances such as 2,3-diphosphoglycerate (abbreviation DPG) [39], the equipping of the erythrocytes

with phytic acid (inositol hexaphosphate, abbreviation IHP) [40] is particularly suitable for the reduction of the O_2 affinity. Since IHP, due to its strong negative charge, does not penetrate the erythrocyte membrane, it is necessary to incorporate this substance according to [41, 42], e.g. in liposomes, and to bring it into the red blood cells in this way [43, 44], or to embark

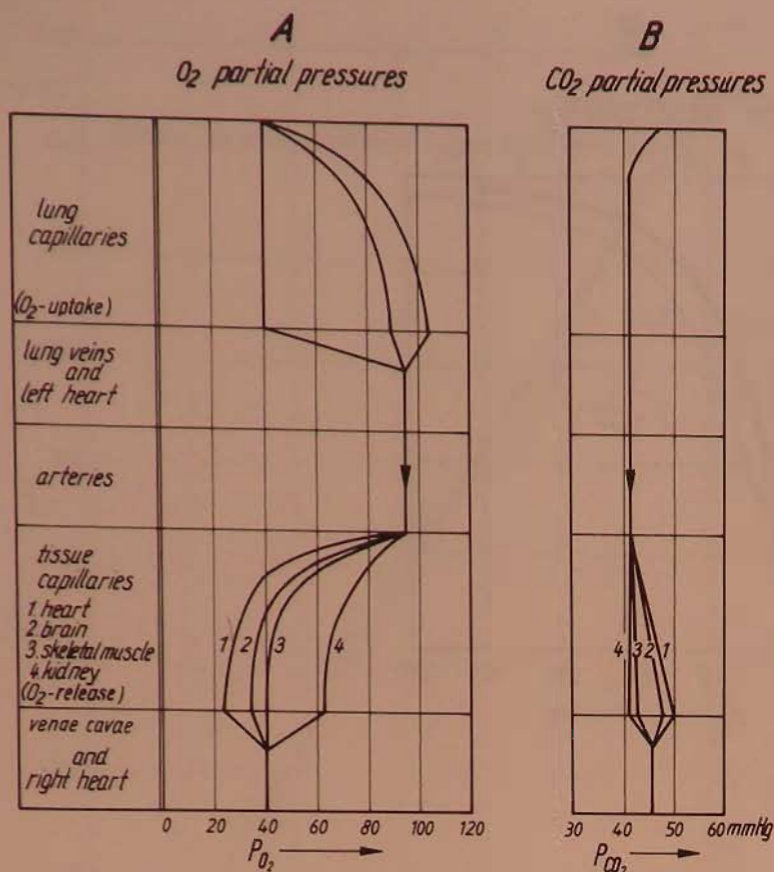


Fig. 9 O_2 partial pressures (A) and CO_2 partial pressures (B) of the blood in the various sections of the circulatory system under resting conditions

on chemical [16] or other ways to overcome the membrane barrier, without losing the IHP effect [45]. Because of its complicated nature and the fact that it is effective for only 60 days, this method has not as yet been of practical significance. It should be pointed out in this section that, according to [46], the DPG con-

centration in erythrocytes is increased by roughly 20 % by intensive physical training. Next to the slight shifting of the O_2 equilibrium curve to the right, caused by this, a flattening of the curve and an increased venous resting P_{O_2} can be observed in competitive sportsmen.

1.1.5 The determination of the resting O_2 status and further characteristic values

1.1.5.1 Definition of the resting O_2 status

The *absolute characteristic value for the resting O_2 status* be defined as the spirometrically determined O_2 absorption of the organism via the lung under conditions of physical rest. Strictly speaking, the O_2 absorption is given as the sum of the two contributions Q_{O_2} and Q'_{O_2} , with Q_{O_2} representing the O_2 transport to the organs and tissues by means of O_2 loading and O_2 discharging of the hemoglobin in the blood circulation, and Q'_{O_2} representing the O_2 transport by direct O_2 diffusion from the lumen of the arterial vessels to special tissues (e.g. arterial walls, vitreous body, cartilage, etc.). As $Q'_{O_2} \ll Q_{O_2}$, it is generally sufficient for consideration of the balance, to use Q_{O_2} alone as an (absolute) characteristic value for the resting O_2 status.

The numerical value of Q_{O_2} is, according to Table 2, a product of three factors. Fast and great fluctuations are only observed in the first

factor, the O_2 saturation difference η of the blood. The momentary resting level of η is therefore a relative characteristic value for the momentary O_2 status, with information content of high diagnostic significance.

The second factor, the *resting cardiac output* normally changes only slowly with training condition and age.

The third factor, the *hemoglobin content* Hb of the blood usually remains roughly constant in the individual case, also over longer time-spans.¹

¹ The hemoglobin content is known to be temporarily reduced to roughly 66 % of its starting level, with the hemodilution method [47]. Nevertheless, a significant increase in the O_2 transport to the body tissue results, particularly because the venous P_{O_2} drops, and the great increase in η and in cardiac output which then occur, greatly overcompensate for the influence of the hemoglobin (hematocrit) reduction.

Table 2 The quality of the O_2 status is approximately equal to energetic state

O_2 transport into body tissue O_2 consumption in body tissue:

$$QO_2 [l O_2/min] = \eta \times COP [l/min] \times Hb [O_2]$$

The meanings:

= Utilization (degree of exploitation) of the O_2 binding capacity of the blood measured at rest

A relative characteristic value, usually applicable for diagnostic purposes, as the resting COP usually only changes slowly with age and fitness, determined by means of the O_2 binding curve of the blood, using measurements of the arterial and venous resting P_{O_2} .

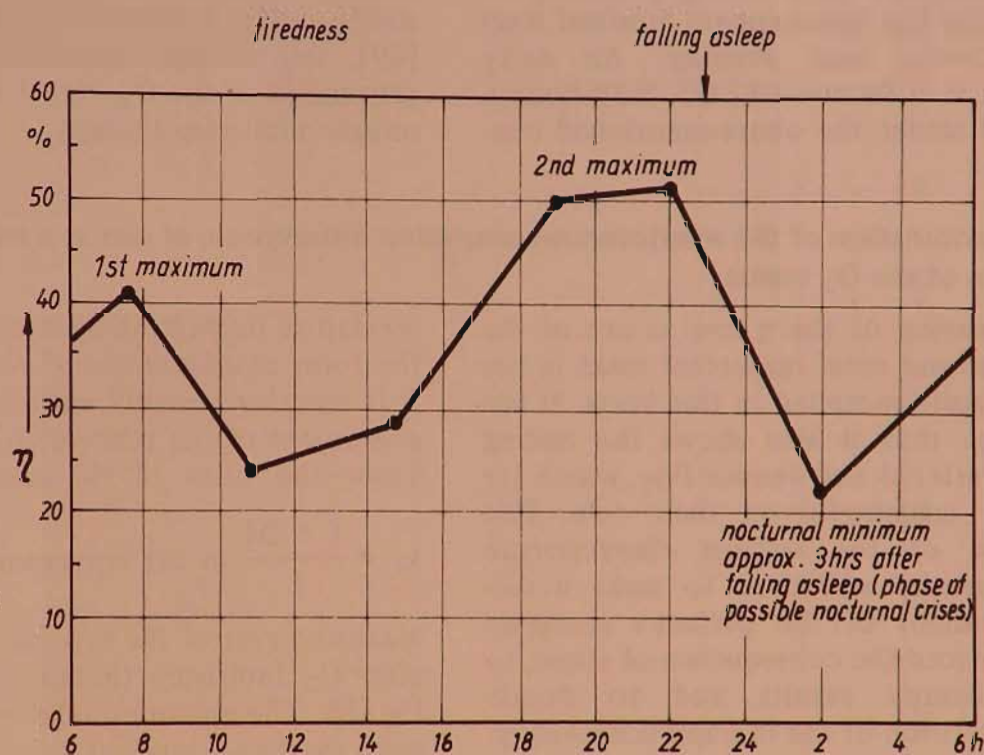
COP = Cardiac output (at rest) = stroke volume SV x pulse frequency f.

Determined, e.g. by spirometric methods, reduced with age, but regenerable to some extent by O_2 MT + exercise.

Hb = Haemoglobin content of the blood. In the individual roughly constant ≈ 160 g Hb/l (1 g Hb binds 1.34 ml O_2) $\hat{=}$ 0.2144 l O_2 /l blood.

A

Measurements of the daily 24-h cycle of the O_2 -saturation difference η in the blood in a healthy male (39 years) treated with O_2 MT. The deviations of η are largely conditioned by alterations in the venous resting pO_2 and are roughly proportional to the deviations of O_2 uptake



B

Representation of the daily 24-h cycle of the mean physiological performance capacity P according to O. Graf [cf. 48]. P stands for percent of variation from daily mean.

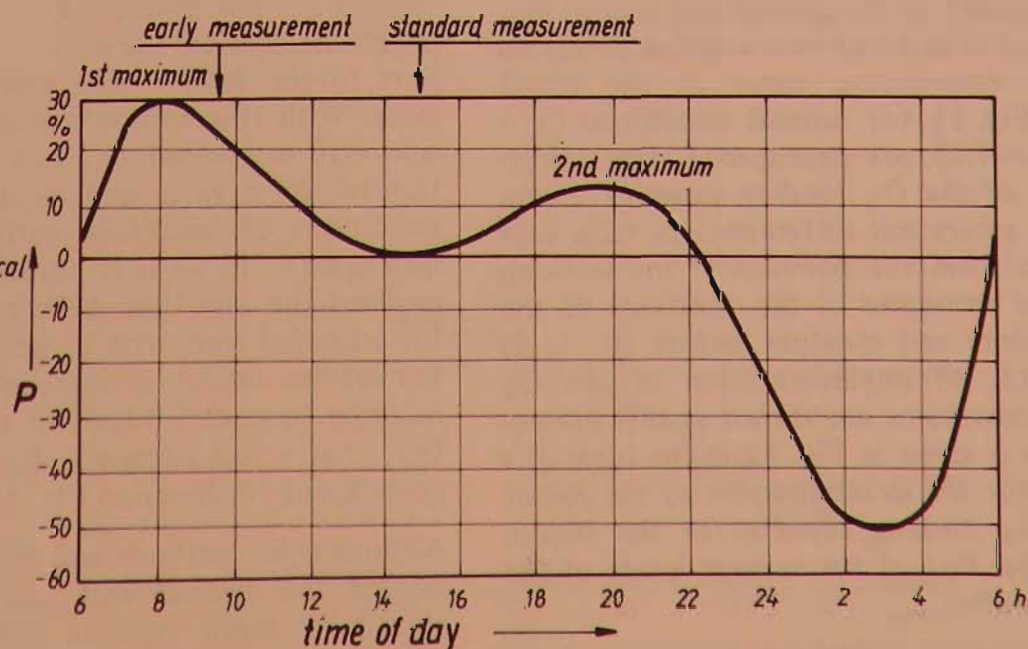


Fig. 10 The occurrence of two maxima and two minima of the energetic status in the daily 24 hour cycle is clearly reflected in the O_2 saturation difference η (A), and also in O. Graf's findings on the course of the mean physiological performance capacity (B)

1.1.5.2 Time of day for determination

The absolute characteristic value Q_{O_2} and the relative characteristic value η of the resting O_2 status change significantly in the course of the circadian cycle. Figure 10 A shows a measurement example of η for this. In Fig. 10 B our measurement is compared with the circadian rhythm of the mean disposition to work, according to O. Graf [48]. For the establishment of the therapy effect, the resting Q_{O_2} or resting η measurements before and after treatment should always be undertaken at the same time of day (and under the same external conditions). We recommend the *standard measurement* to be taken at 15.00 hours (14.00–16.00 hours), at rest and in a sitting position, representative for the approximate *minimal level between morning and evening*. An early measurement at 9.30 hours (7.00–9.30 hours), accomplished under the above-mentioned con-

ditions, seems to be representative for the maximal level between morning and evening.

If the unique opportunities, which lie in the determination of the resting O_2 status for diagnostic purposes, are to be used, it is particularly important to standardize the time of day for the determination (e.g. 14.00–16.00 hours).

The deep minimum of the O_2 status approximately 3 h after falling asleep is noteworthy in Fig. 10. It is the time point at which circulatory disorders, cardiac arrest, myocardial infarction in risk patients occur with greater frequency. The low level of this nightly minimum can usually be somewhat countered by a cup of strong coffee immediately before falling asleep [49], and strongly countered by a lasting improvement in the O_2 status with the aid of the oxygen multistep therapy.

1.1.5.3 Determination of the arteriovenous saturation difference η at rest as a relative characteristic value of the O_2 status

The determination of the η level is one of the most frequent and most important tasks in the use of the results compiled in this book. It has the advantage that it also shows the resting levels of the arterial and venous P_{O_2} , which are often highly meaningful on their own. *The determination of the relative characteristic value η* is usually sufficient to make a diagnostic assessment of the patient's energetic reserves, to record the consequence of stress, to document therapy results and to decide whether a repetition of the therapy is necessary.

By measurement of the arterial and venous P_{O_2} in conditions of rest, the two working points on the HbO_2 dissociation curve of the blood shown in Fig. 11 for normal conditions ($T = 37^\circ C$, $pH = 7.4$), are determined. The *utilization factor of the O_2 binding capacity of the blood* (O_2 saturation difference) in each case can be seen from the position of the working points. Five examples of the positions of the working points and η -values before (0, 1, 2) and after (3, 4) implementation of the O_2 multistep procedures are shown in this presentation. Help is given in Fig. 12 in the form of a *nomogram for the determination of the factor η of the O_2 binding capacity* of the blood, dependent on P_{O_2-art} for various levels of the mixed central P_{O_2-ven} .

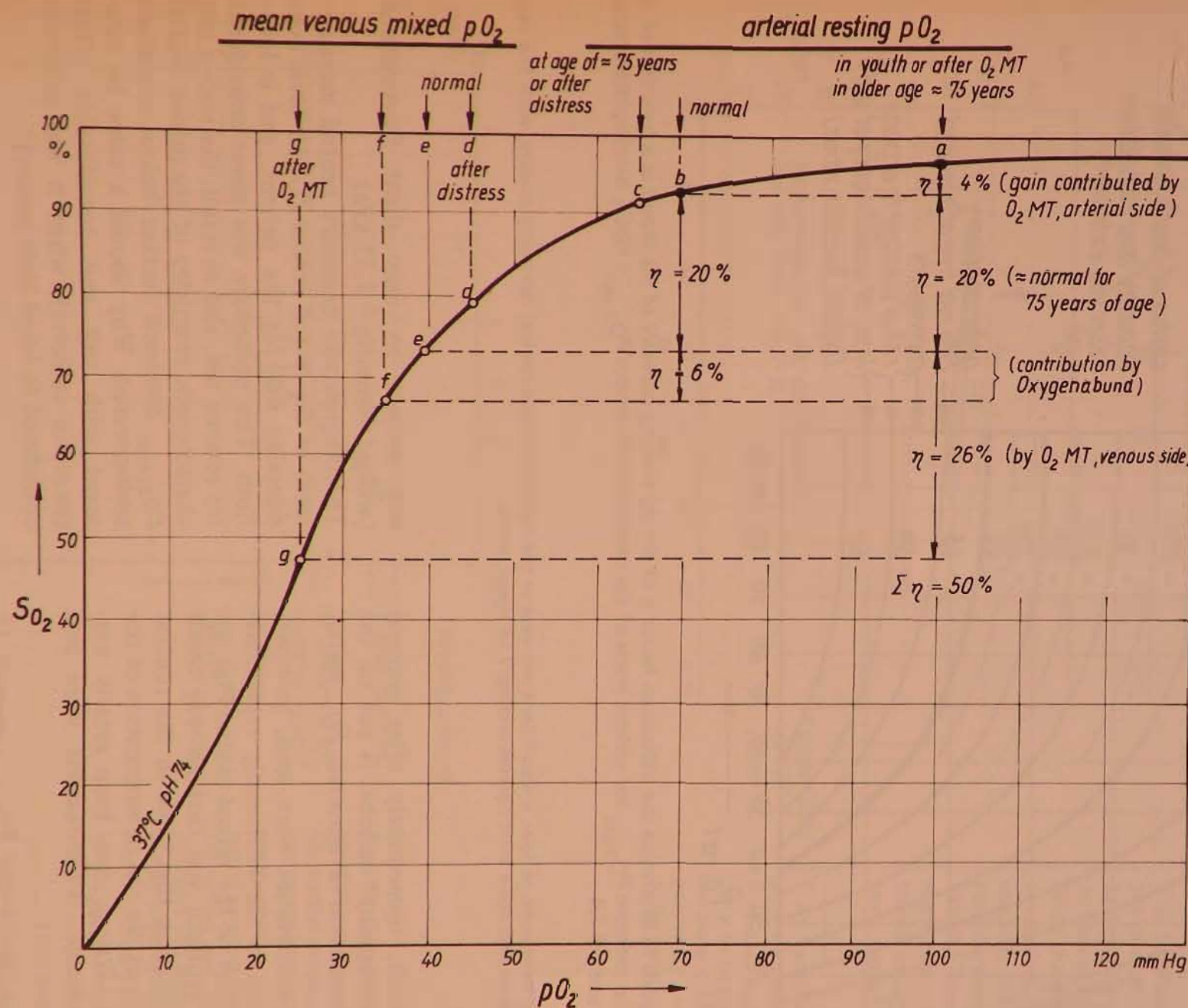
The cardiac output (COP) is the product of the stroke volume V_s and the pulse frequency f . In resting conditions the stroke volume remains virtually uninfluenced. The naturel counter-

regulation in η -changes almost exclusively takes the form of *adaptation of the pulse frequency*. It is therefore usually sufficient for the stricter assessment of the relative O_2 transportation, to know the value of the relative pulse change

$$k_f = \frac{f + \Delta f}{f} \text{ in the corresponding change of } \eta.$$

Measurements of the η /pulse counter-regulation after O_2 multistep therapy are summarized in Fig. 13. The measured relative drop in the pulse only reaches a level of $k_f = 0.91$, even after a tripling of the η -value. *The η -value therefore largely determines the volume of the O_2 transport to the body tissue under normal conditions*. With this approximation, further discussion may be limited, as a rule, to the consideration of the η value and its dynamics. Only in conditions of weakness with very (too) low η -values ($< 15\%$) is it necessary to take into account the fact that the organism then reacts for a limited time with a significant increase in the cardiac output (increase in pulse frequency) in order to ensure a level of O_2 transportation Q_{O_2} that is just adequate. Examples of this are cases 8 and 10 shown in Fig. 15.

Although the methods and techniques of determining the arterial and venous P_{O_2} are discussed in depth later in the book, it seems necessary to mention at this stage the hitherto apparent principle difficulties. The sufficiently accurate measurement of the resting P_{O_2-art} is today problem free, usually made from a drop



Utilization of the O_2 -binding capacity η in a normal person of about 75 years

combination of steps	working points	η	duration
0 after severe distress (crisis) (example)	c d	13%	until rehabilitation
1 before O_2 MT	b e	20%	permanent
2 after permanent daily intake of Oxygenabund	b f	26%	permanent
3 after 36 h O_2 MT	$\approx$ a g	$\begin{matrix} 4 \\ +20 \\ +26 \\ \hline 50\% \end{matrix}$	permanent
4 after 15 min O_2 MT quick procedure variant GK 2-I	$\approx$ a g	$\begin{matrix} \approx 2 \\ +20 \\ +26 \\ \hline \approx 48\% \end{matrix}$	permanent
O_2 transport to the body tissue $Q_{O_2} \sim \eta \cdot K$; $K \approx 0.9 - 1.3$ (the factor K considers changes of the cardiac output and the pulse rate)			

Fig. 11 Changes in the utilization coefficient η of the O_2 binding capacity of the blood exemplified in a 75-year-old male subject before and after O_2 MT treatment (either variant GK 4-I, or GK 2-I)

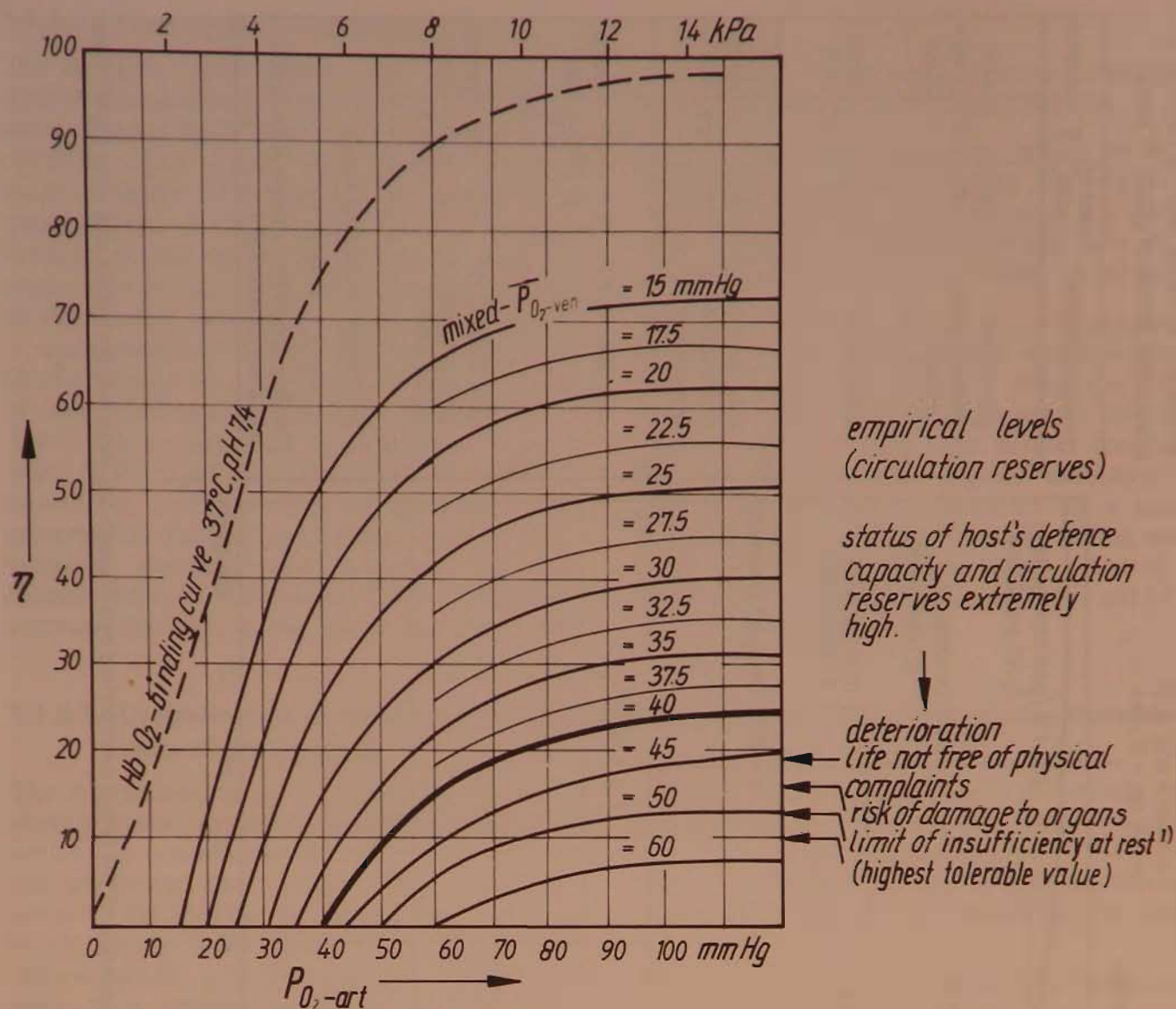


Fig. 12 Nomogram to determine the utilization factor η of the O₂ binding capacity of the blood as a function of the arterial O₂ partial pressure P_{O_2-art} for various levels of the central mixed venous P_{O_2-ven} . HbO₂ binding/dissociation curve for 37°C and pH 7.4

¹ When η values have sunk so low, a significant increase in the cardiac output (pulse) normally occurs, with the result that the values in this scale shift correspondingly to lower levels

of blood which, immediately after removal from the "arterialized" earlobe, is put on the indicator electrode of a universal P_{O_2} meter.

Fundamental difficulties were seen, however, in the question of the sufficiently representative measurement of the mixed central P_{O_2-ven} . The greatest problem was that no way could be seen of including this value in the routine blood gas analysis. So the determination of the mixed central P_{O_2-ven} has been greatly neglected in medicine. Two reasons were particularly decisive here:

1. The magnitude of the P_{O_2-ven} seemed to give little information, because it was usually assumed that the mixed central venous P_{O_2}

was subject to only slight fluctuations (around 40 mmHg $\hat{=}$ 5.33 kPa).

2. The theoretically necessary central measurement of the mixed venous P_{O_2} involves considerable risk for the patient, and is laborious. This procedure was never considered for routine use, and as result, the strong and characteristic reactivity of the mixed central P_{O_2-ven} , discussed further below, remained undiscovered. Why should a value be measured with risk and considerable effort (sweep-in catheter), when it was generally considered to be of little interest?

Even in the investigation of the effects of the HOT* method (reinfusion of the patient's own

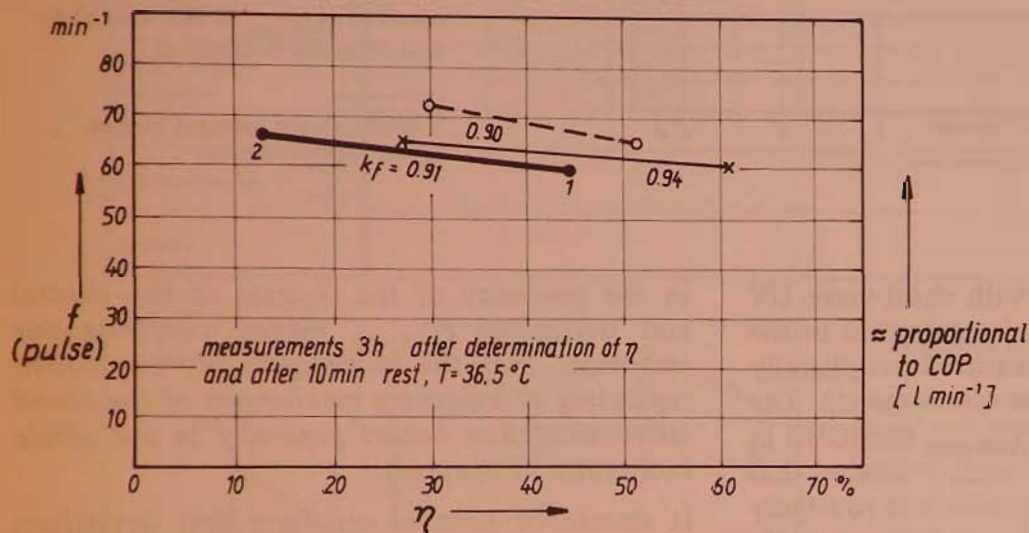
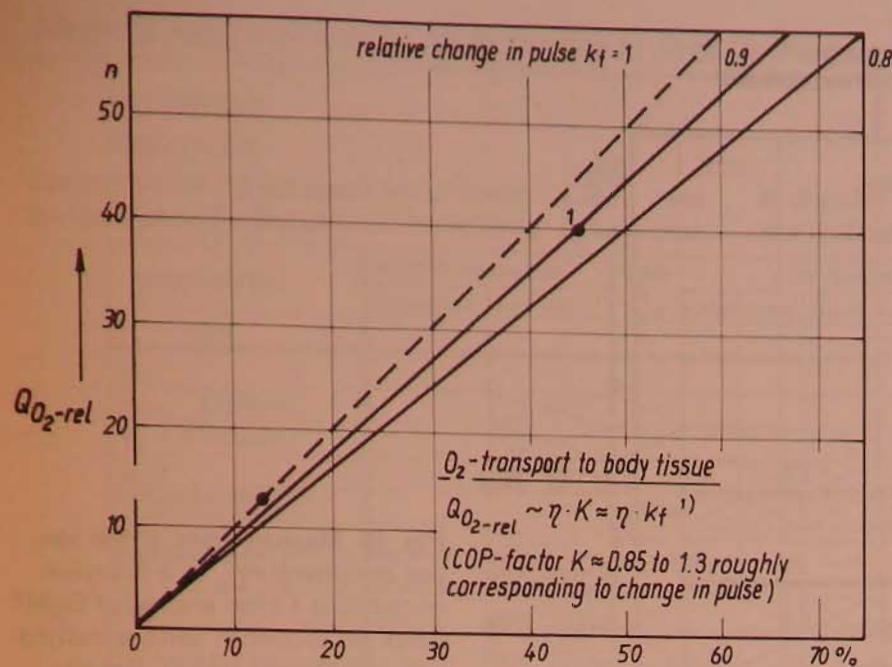


Fig. 13 Measurement of the relative drop in pulse k_f (roughly proportional to cardiac output COP) when the utilization factor η of the O_2 binding capacity of the blood is considerably increased. Result: The value of η mainly determines the O_2 transport Q_{O_2} into the body tissue²

¹ At rest, the stroke volume $v = \text{const}$

² The increase in COP is only to be considered at values $\eta < 15\%$ accompanied by considerable pulse acceleration

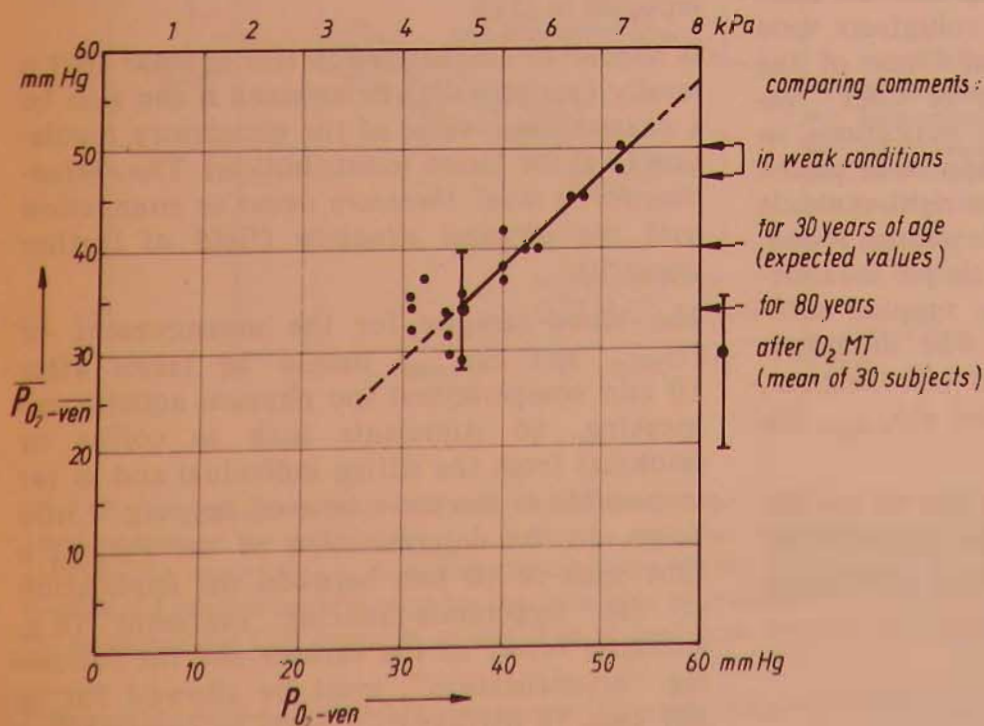


Fig. 14 Correlation between the centrally measured mixed venous O_2 partial pressure P_{O_2-ven} and the peripheral venous O_2 partial pressure P_{O_2-ven} measured in blood samples taken from the un-staunched and unstrained vena cubitalis (no asymmetry); all measurements accomplished under resting conditions¹; mean values of 19 individuals (Dauterstedt et al. [51]), see also [54, 55]

¹ Under O_2 MT conditions (during O_2 application) a somewhat different relationship, as in [51], is to be applied

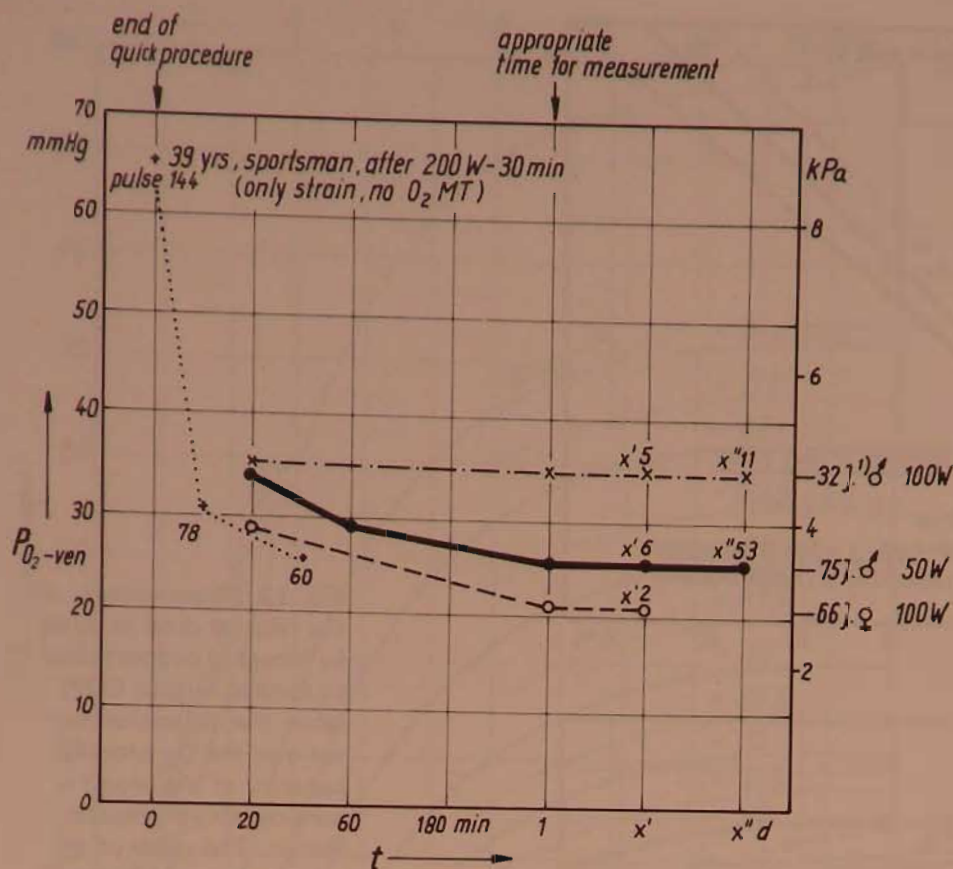


Fig. 15 Measurement of the venous peripheral PO_{2-ven} as a function of the time t after ending of O_2MT quick procedure in various individuals at different strains. Result: the appropriate time for measurement of PO_{2-ven} is one day after end of quick procedure

¹ Slight strain relative to age; quick normalization

blood after its irradiation with short-wave UV light) [50], we found typical regularities in the behaviour of the PO_{2-ven} measured peripherally from the vena cubitalis (no tourniquet!). The observed dynamics of the PO_{2-ven} measured in resting conditions from the arm, indicated that even this simple procedure, which is routinely reasonable for the patient, can lead to sufficiently representative values. Therefore, the comparison at rest and in normoxia between the mixed central PO_{2-ven} and the peripherally measured PO_{2-ven} was carried out as summarized in Fig. 14 [51]. The volunteers were patients from the Radiological Clinic of the Medical Academy of Dresden or CMT¹ patients, in whom due to other indications an intracardiac catheter had already been placed in the arteria pulmonalis or the right ventricle of the heart. From the minor deviations found, it follows that the relatively simple measurement from the arm generally supplies sufficiently representative values. The deviations remain small as a rule, compared with the great, reactive changes in the resting PO_{2-ven} discovered and described below.

Since these great changes occur due to the discovered switching process of the microcirculation, the sufficient correspondence ascertained

in the tendency of the courses of the central and peripheral PO_{2-ven} values, confirms our statement that the bioenergetically controlled regulating or switching mechanism of the blood microcirculation occurs generally in the whole body (also in the arm).

It should be pointed out here that deviations between the levels measured from the unrestrained vena cubitalis and the levels measured centrally from the arteria pulmonalis of about the same low level as in Fig. 5, were also reported in [52].

It should be emphasized in this context that a locally (peripherally) determined η can also be a characteristic value of the circulatory regulation (e.g. for blood redistribution). The evaluation for η must therefore occur in connection with the physical situation (field of further research).

The blood samples for the measurement of PO_{2-art} and PO_{2-ven} should be taken after 10 min complete rest (no physical activity, no speaking, no stimulants such as coffee or smoking) from the sitting individual and as far as possible at the same time of day, e.g. 15.00 hours. In the determination of the PO_{2-art} a time span of 10 min between the application of the hyperemia-inducing ointment (e.g. Finalgon forte) to the earlobe and the following "arterialization", must be allowed for in any case. In particular, it must be remembered

¹ CMT = cancer multistep therapy

Medical record on the O₂ MT according to Prof. Dr. med.h.c. Manfred von Ardenne

Cure institution: _____ No: _____
 Name of patient: _____ Age: _____ Years Sex: _____
 Cure procedure GK 3-IV with separate exercise training O₂ flow l/min No. of sessions Total no. of hours h
 Quick procedure GK 2 with simultaneous exercise training O₂ flow l/min No. of repetitions Total no. of minutes min

measurement time	immediate measurement		middle of cure	after cure procedure					
	before inhalation	during inhalation		= 2 days	1 week	2 weeks	1 month		
date									
P _{O₂-art}									mm Hg
P _{O₂-ven} peripheral									mm Hg
η (~ O ₂ -transport)									%
pulse									1/min
quick procedure, physical strain e.g. with bicycle ergometer			repetition						watt
blood pressure RR									mm Hg
P _{CO₂}									mm Hg
pH									
base excess BE									mval/l
transaminases SGOT									U/l
transaminases SGPT									U/l
triglycerides									mmol/l
cholesterol									mmol/l
exercise training									capacity
effects of therapy objective									
effects of therapy subjective									
remarks									

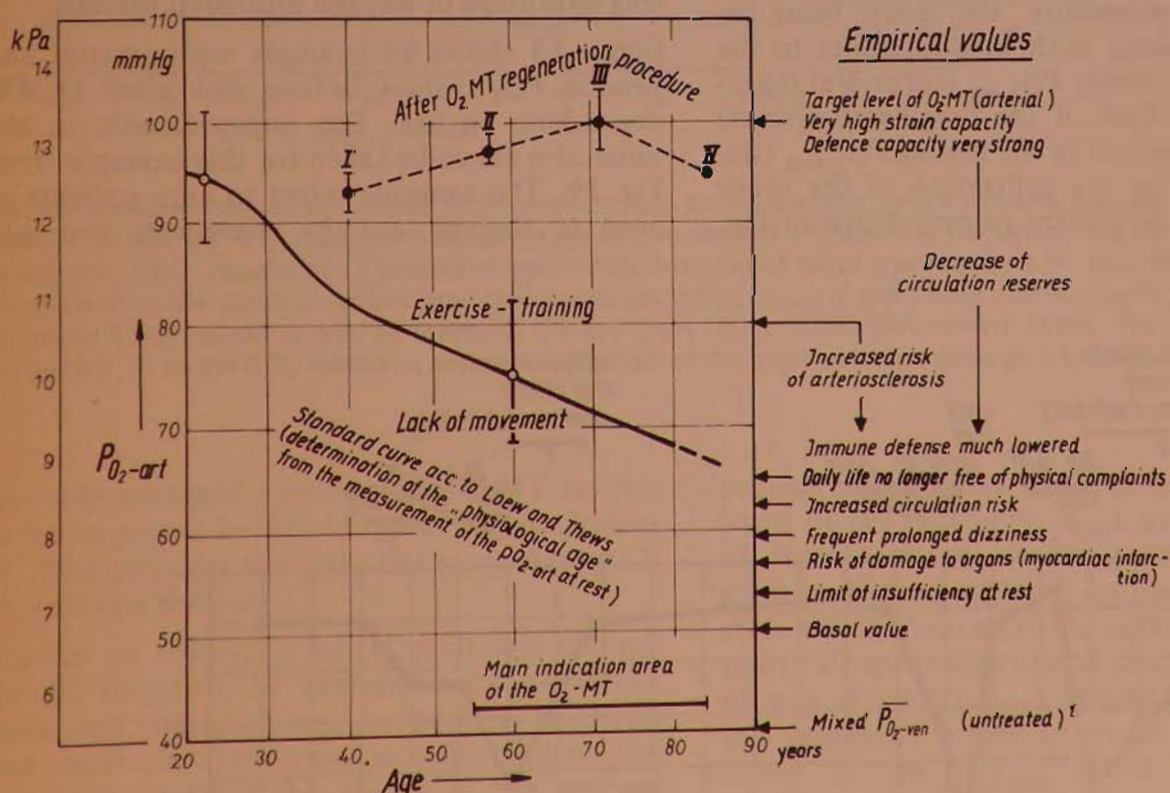


Fig. 16 Average dependence of the resting arterial oxygen partial pressure P_{O_2-art} on age, and results of the permanent increase of the reduced P_{O_2-art} at rest, by means of the discovered O₂MT procedure in patients of 4 age groups (I–IV). The resting P_{O_2-art} is a characteristic value for the degeneration and regeneration of the lung system. The η -value is a relative guiding value for the O₂ supply of the organism (energetic situation and general condition). The O₂ uptake or the CO₂ emission, at rest, is to be used as an absolute characteristic value (see appendix)

[†] Reduction by means of O₂MT procedures. Then the "empirical value" scale is also brought down

that following completion of the quick procedure with its physical exertion, the renormalization of the cardiac output varies in time required according to the individual exertion. According to the measurements of the course of the peripheral PO_{2-ven} in Fig. 15, an interval of one or two days after the end of the procedure seems to be a suitable time for measurement.

All PO_{2-ven} measurements given were carried out on the same (usually the right) arm. In patients with single-sided exertions or treatment, a measurement from the vena cubitalis of the other arm should also be undertaken, in order to take into account the "vegetative asymmetry", to which A. Pischinger [53], in particular, has drawn attention. Findings of this type show that the energetic (i.e. O_2 sensitive) control of the switching process of the blood microcirculation is to be seen as standing in interplay with *vegetative-nerval and vegetative-humoral regulating mechanisms* of the peripheral circulation. This viewpoint could explain the effect of various stressful factors, such as psychic factors, on the size of the arteriovenous O_2 saturation difference η .

The procedure success is objectified from measurements after the implementation of the O_2 multistep procedure, the result being recorded numerically both with reference to the increase in the resting PO_{2-art} (successful regeneration in the field of the lung-heart system) and to the reduction in the resting PO_{2-ven} (improvement in the O_2 utilization of the other body tissue). The patient record shown in Fig.

16 was designed in order to simplify the documentation, and the patient should be given a copy of it after the findings have been entered. By means of measurements at certain time intervals and particularly after severely stressful events, especially after infections, operations etc., it can be quantitatively judged whether a *repetition of the O_2MT procedure* is to be advised or not. Furthermore, such measurements make possible a statement as to whether good PO_2 levels can be brought about naturally by a change in lifestyle (e.g. transition to phases with daily heavy physical exertion).

The measurement of the resting PO_{2-art} alone is often sufficient as a basis of the decisions to be made, or for controls, because the inverse changes in the resting PO_{2-ven} are triggered by the same capillary switching mechanism. Their dynamics are therefore an approximate mirror image of those of the resting PO_{2-art} . Fig. 17 shows an example of the *implementation of a favorable lifestyle over a longer time span with reference to the PO_{2-art}* by means of interplay between measurements of PO_{2-art} and counter-measures. The opportunity to record quantitatively momentary energy reserves, indications, therapy results and cure successes is a fascinating advantage of oxygen multistep therapy.

Figure 18 shows an example with arterial and venous PO_2 values before and after O_2MT , dependent on age. The improvements in the value of η are to be taken for this example from Fig. 19. The example refers to cure patients in need of therapy, for the objectively and sub-

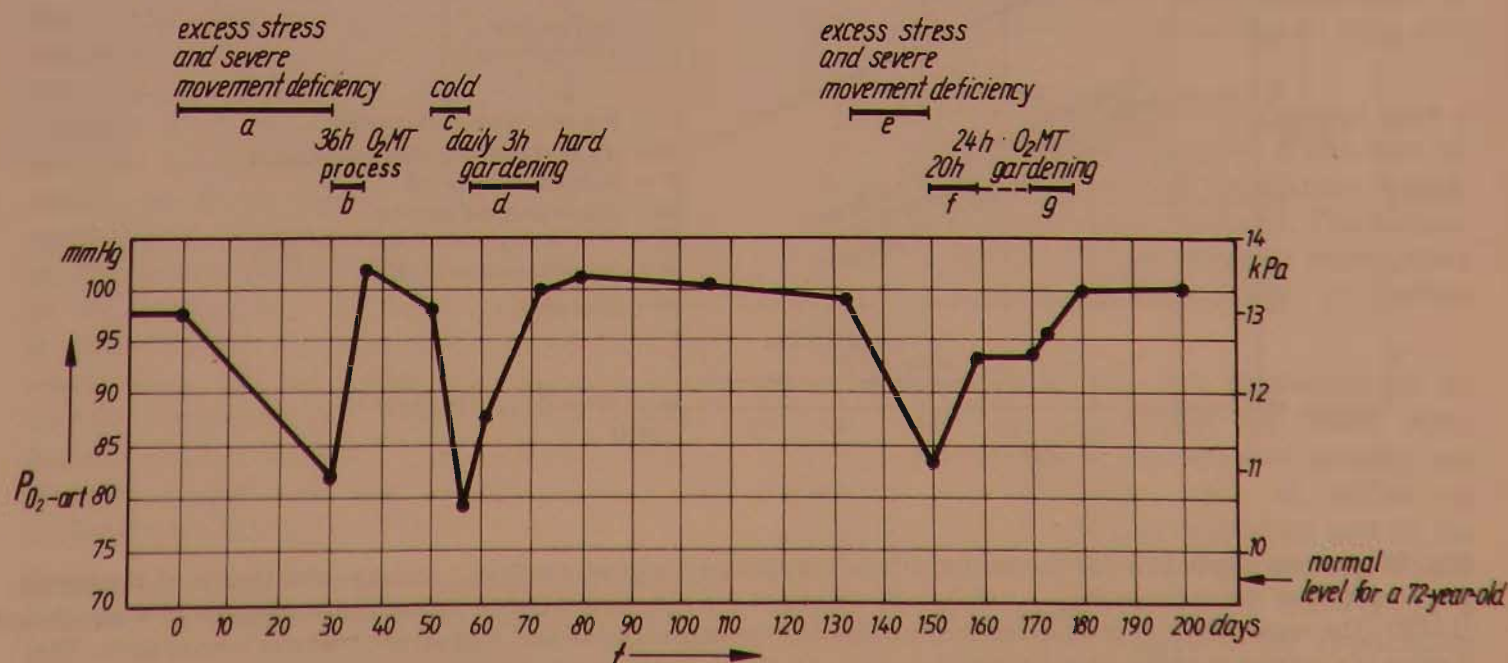


Fig. 17 Example of the reactivity of the lung-heart system, and of healthy PO_{2-art} controlled lifestyle. Measurements of the change of the arterial resting PO_2 in a 72-year-old man treated with the O_2MT , variant GK 4-I, dependent on excess stress (a, e) or a common cold infection (c) followed by regeneration measures (b, d, f, g)

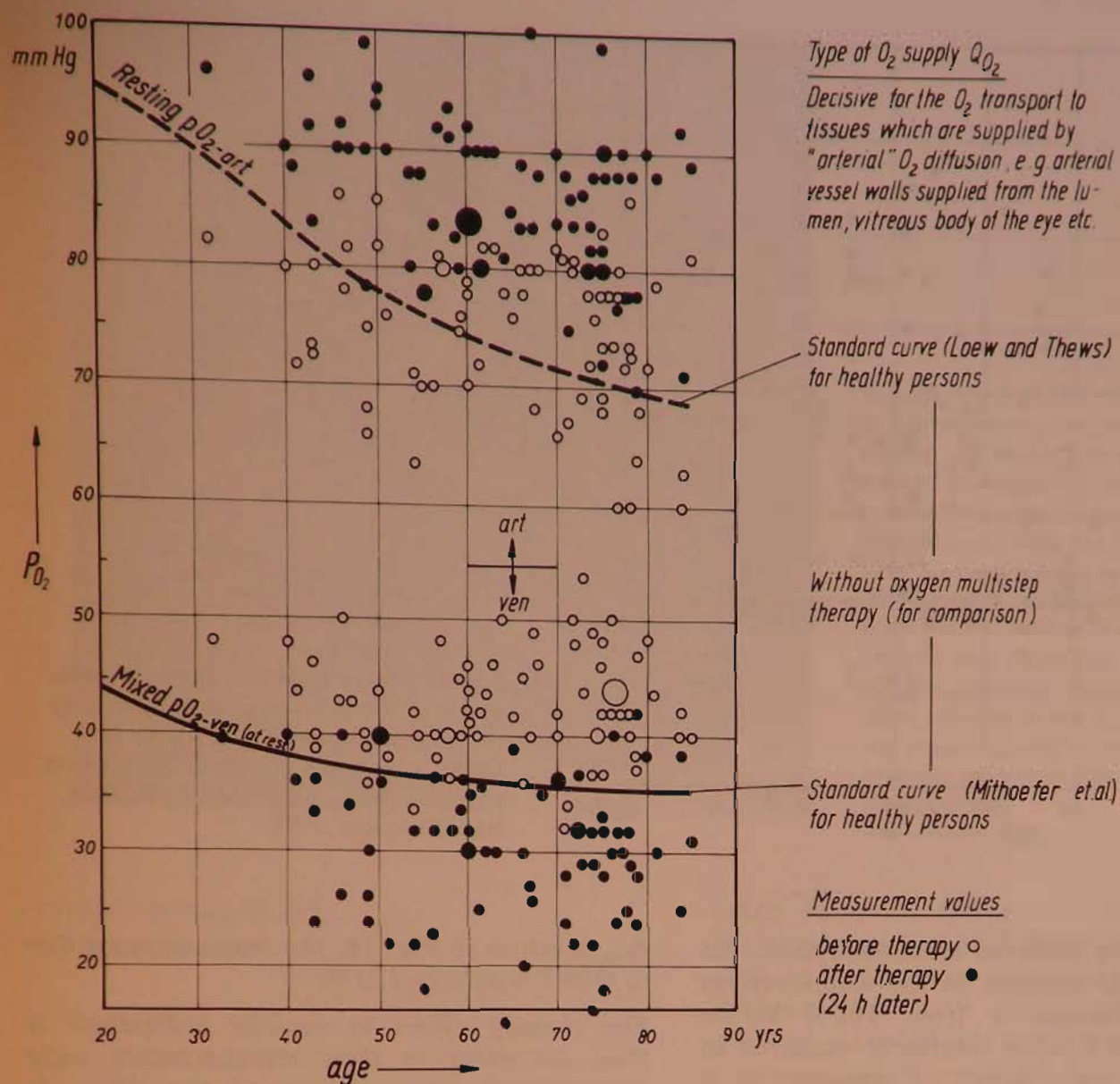


Fig. 18 Measurements of the arterial and venous oxygen partial pressure before and after oxygen multistep therapy (usually variant GK 4-I), dependent on age, in patients in need of treatment at the sanatorium of Dr. H. Wolf, Bad Wildungen, FRG. Results of 72 successful treatments. Number of failed treatments: 8 (= 11%). Measured values in comparison to the expected values (standard curves according to Loew and Thews and Mithoefer, respectively). Increased η (O_2 uptake at rest) by means of therapy from 100 to 230% (80 patients; 1985). The increase in the O_2 uptake, or in the CO_2 release, is approximately half of the increase in the value of η (see appendix)

jectively strongest effects of the O_2 MT are not to be expected in individuals in full possession of their physical strength, but in weakened, ill or suffering patients.

Studies on the effect of O_2 multistep therapy should therefore be performed on physically weakened subjects¹, e.g. on patients in clinics and sanatoria. This view is confirmed by the measurements and the course of the two expected curves in Fig. 18. Both fields here, with the values measured *before* therapy, both below (PO_{2-art}) or above (PO_{2-ven}) the respective ex-

pected curves (with their in places very high levels of the resting PO_{2-ven}), are an expression of the weakened condition of most patients studied. Fascinatingly, it can be seen here that after O_2 MT treatment the measured values for nearly all age groups can on average be found to be way above (PO_{2-art}) or way below (PO_{2-ven}) the respective expected curve. The mean increase in the PO_{2-art} here is approximately 10–20 mmHg (1.4–2.8 kPa), whilst the mean reduction of the resting PO_{2-ven} is approximately 10–15 mmHg (1.4–2.1 kPa). A very significant increase in the O_2 status (η -value) of the patients is reflected in these numbers, correlating with impressive records of objective and subjective improvements in the condition of health of the individual patients. Almost the same results, admittedly with a smaller number

¹ But not on permanently bedridden patients who are incapable of sufficient movement (lack of the 3rd step of therapy; for such patients, HOT* is indicated as an adjuvant step)

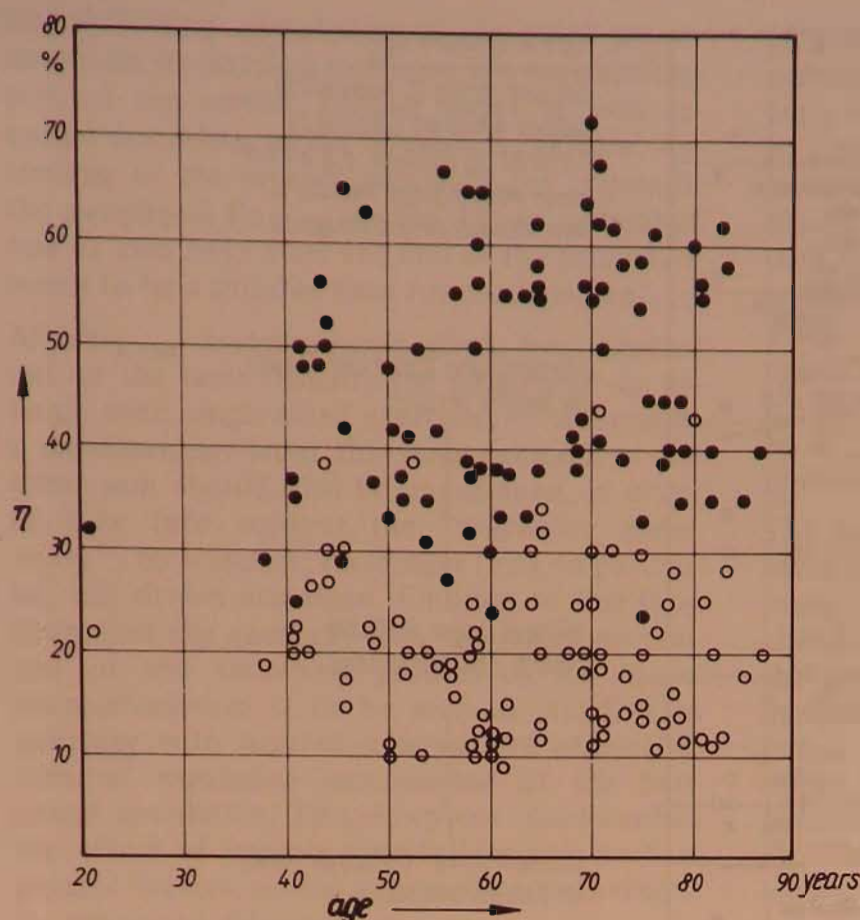


Fig. 19 Measurement of the utilization factor η of the oxygen binding capacity of the blood before (○) and after (●) O_2MT , dependent on age, in 88 patients of the sanatorium Dr. med. S. H. Wolf, Bad Wildungen, FRG

of patients, were achieved in another clinic. An average (lasting) increase in the arteriovenous saturation difference η from 100% before therapy to 239% after treatment occurred in the Bad Wildungen group of patients. In a smaller patient sample in Bad Füssing the increase after therapy was 230%. It can therefore be established that *in patients in about the same degree of need of therapy the same improvements of the O_2 status to about 230% occur. In healthy volunteers and with the same*

PO_2 levels as in Fig. 18, the mean increase due to O_2MT would be 133%.

The therapy effect in healthy individuals is thus, according to these measurements, only approximately one quarter of the effect in weakened patients.

It follows from this that in the testing of the effect of the oxygen multistep therapy, the composition of the patients' sample plays a decisive role.

1.1.5.4 Determining the resting O_2 uptake of the organism as an absolute characteristic value of the O_2 status

In the framework of research and in special cases in O_2MT treatments, when cardiovascular training is combined with the procedure and then the resulting changes in the cardiac output are to be documented, a codetermination of the O_2 uptake, at rest, of the organism almost becomes a necessity.

A series of methods, invasive and non-invasive, has been designed, e.g. [56, 57], for the direct determination of the cardiac output (at physical rest and under exertion). After previous experiments with the impedance-cardiographic method, which proved not to be particularly suited to the determination of absolute values of the cardiac output, the *spirometric unit* in Fig. 20

was developed for direct measurement of the resting O_2 uptake. The arrangement also allows the determination of the maximal O_2 uptake and CO_2 production of the organism. The principle discussed below has the advantage that, in inhalation, we are not dealing unphysiologically with pure oxygen, but with air of natural composition. The arrangement shown makes possible the extremely accurate measurement of the O_2 uptake at rest and a surprisingly accurate calculation of the absolute levels of the resting cardiac output with the help of the following well-known equation resulting from Table 2:



Fig. 20 View of the measuring assembly for the determination of the O_2 uptake at rest and of the maximal O_2 uptake of the organism, as well as of CO_2 production at rest. Development: Manfred von Ardenne Research Institute. Simultaneously with our own development, an Oxycon-4 instrument from the Fa. Hellige, Freiburg/Br. (FRG) was put into operation in order to record the measured values of the lasting great increase in the O_2 absorption of the organism, and of the CO_2 emission after O_2 multistep therapy as given in the appendix

$$\text{cardiac output (COP)}_{[l \cdot \text{min}^{-1}]} = \frac{\text{resting } O_2 \text{ uptake } [l \cdot \text{min}^{-1}]}{\eta \cdot 0.2144_{[O_2]}}$$

The value of η is determined immediately after measurement of the O_2 uptake, in order to exclude the possibility of errors due to the discovered circadian rhythms in the 24 h cycle (Fig. 10). If the Hb value of the patient is known, the product of the individual Hb and the factor $1.34_{[ml \text{ } O_2 \text{ per g Hb}]}$ should be used instead of the coefficient 0.2144. The standard measurement of 15.00 (between 14.00 and 16.00 hours), resting and sitting, roughly represents the *minimal level* between morning and evening. The early measurement at 9.30 (between 7.00 and 9.30 hours), resting and sitting, is roughly representative for the *peak level* between morning and evening.

Figure 21 A shows typical examples of the increase in the O_2 uptake at rest due to the 36 h 18 day O_2 MT procedure discussed below, both without (variant GK 4-I) and with cardiac training (variant GK 4-II).

The extent of the contributions of the increase in O_2 uptake under various conditions can be

taken from the spirometric measurements of the uptake in Fig. 21 A (cases of untreated persons and volunteers previously O_2 MT treated without and with cardiopulmonary minimal training included in the study). In the case examined there resulted for the male aged 77 years through O_2 MT alone a lasting increase of the O_2 uptake to 161% and through O_2 MT with cardiac training, an increase in the O_2 uptake to 188%. According to Fig. 19 B, the arteriovenous O_2 saturation difference η increased to 209% due to O_2 MT with cardiac training. The improvements in pulse frequency, stroke volume and COP by the two O_2 MT variants can be seen from Figs 21 C, D and E.

Towards the end of the 36 h 18 day treatment (O_2 MT and heart training) the curves in Figs 21 A, B, D and E show the shift of the operating point into a range with saturation character. It can be concluded from this that the chosen combination of type and dosage of the cardiopulmonary minimal training (O_2 , Alupent, physical exertion without extra O_2) have been successful in achieving the desired training effect in the heart without further time expenditure in the framework of the 36 h 18 day O_2 MT standard procedure.

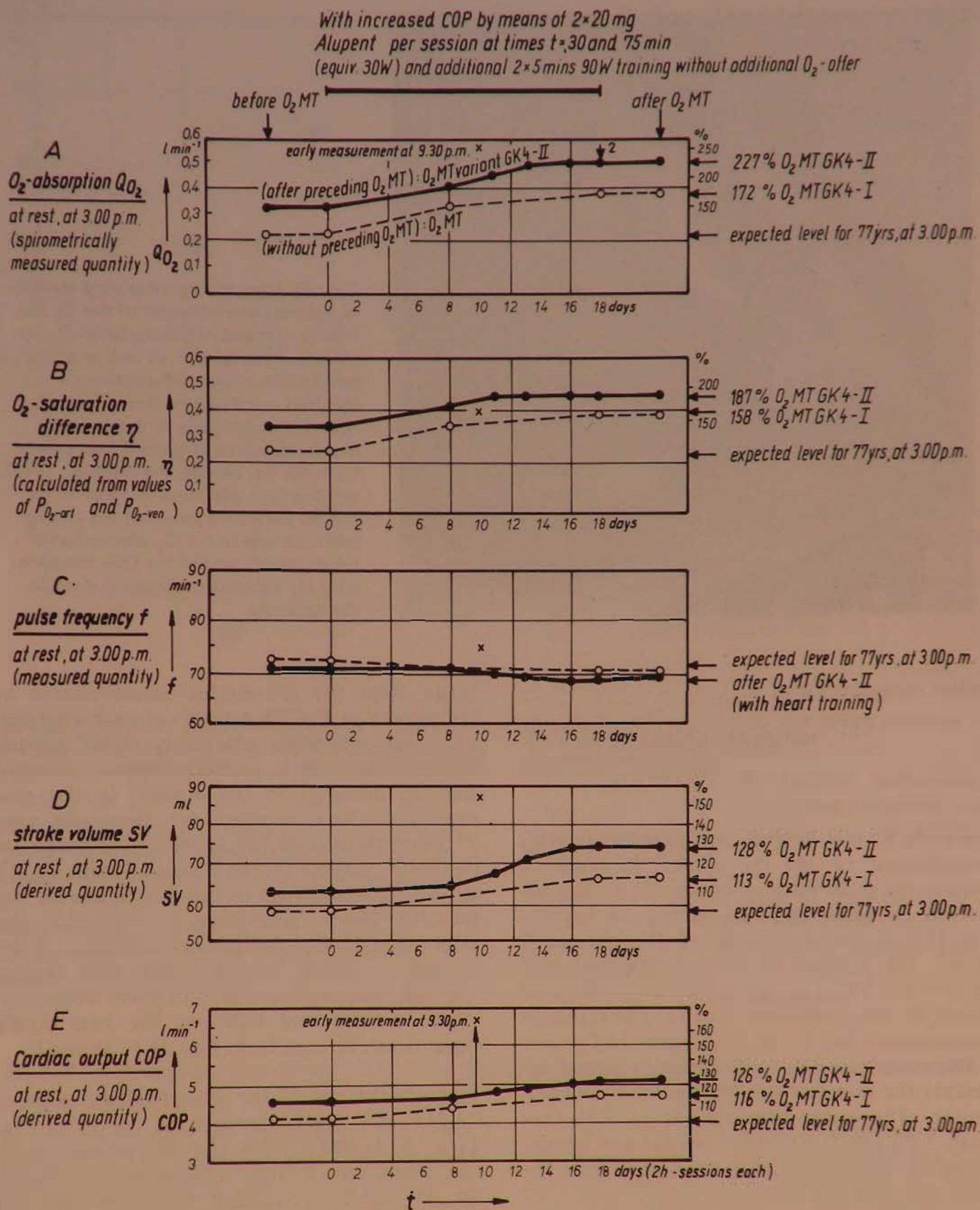


Fig. 21 Examples of the improvements in O_2 uptake Q_{O_2} (A), the O_2 saturation difference of the blood η (B), the pulse frequency f (C), the stroke volume SV (D) and the cardiac output COP (E) by means of the 36 h 18 day O_2 MT (with COP increase during the 2 h session by means of 2x25 min cardio-pulmonal minimal training¹ without O_2 inhalation) Variant GK 4-II. Males of the age group 65–80 yrs with and without preceding O_2 MT treatment and training

¹ Minimal training adapted to age and condition of the individual (e.g. on bicycle ergometer)

1.1.5.5 Determining the maximal O_2 uptake as a characteristic value of the energetic reserves of the organism

The maximal oxygen uptake is an indicator, used particularly in sports medicine, of the aerobic performance capacity of the organism. It is measured when the individual is subjected to continuously increasing strain with an ergometer. When the state of exhaustion is reached, the oxygen uptake levels off. The numerical value of O_2 uptake in the plateau phase is an indicator of the maximum O_2 uptake or of stamina performance capacity. This figure is diagnostically very informative, as it can also be seen as a kind of *characteristic value of the energetic reserves* of the organism. It would therefore be desirable for measurement devices for the routine determination of the resting O_2 uptake and the maximal O_2 uptake to go into large-scale production in the not too distant future.

The expected curve for the maximal O_2 uptake Q_{O_2} -max dependent on age in normal persons can be seen in Fig. 22. The course of the curve shows that this characteristic value drops continuously and steeply after the age of about 20. At the age of 80 the figure is only approximately 42% of the maximum in youth. The closed circles entered give an idea of the mean

variation, and the points marked with a cross were obtained from senior sportsmen. It can clearly be seen that the reduction in the maximal O_2 uptake occurs much more slowly in elderly, physically active persons than in normal persons. The documented result is a serious warning to able-bodied persons not to neglect regular training (cardiovascular training) even in later years [58].

The lower part of the same figure shows the expected curve for the resting O_2 uptake dependent on age. On the basis of the level of the youthful age of 20–25 years, a drop in the resting O_2 uptake, e.g. at the age of 80, of approximately 62% can be seen. In physically active persons of the same age group, the respective value drops to about 60–70% of the maximum. At the bottom of the same figure, measurements of the resting O_2 uptake after implementation of the O_2 MT have been entered as typical examples.

It seemed advisable for practical reasons to design the measuring set-up in such a way that both the maximal and the resting O_2 uptake could be measured by the same apparatus. This

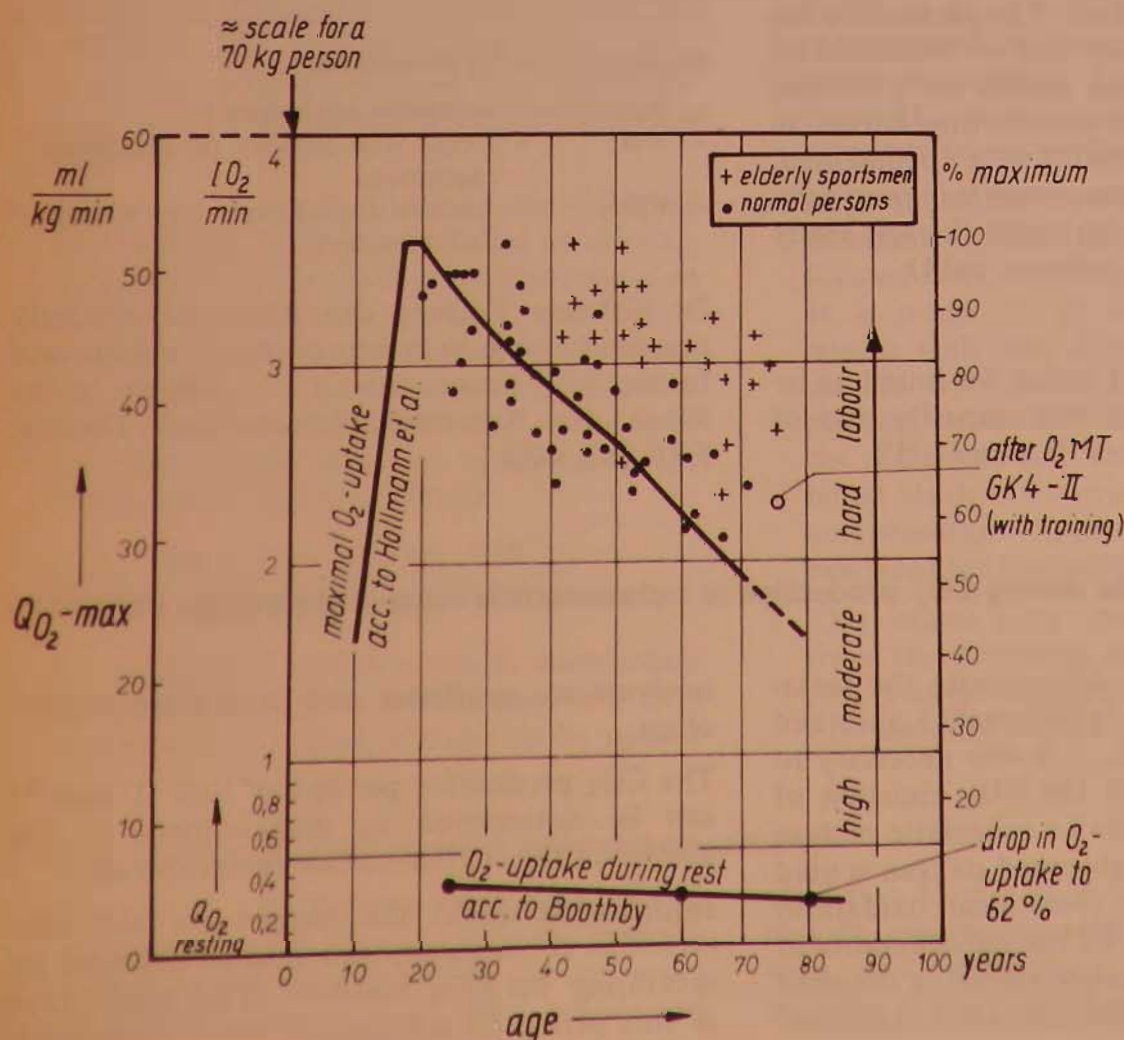


Fig. 22 Maximal O_2 uptake Q_{O_2} max as characteristic value of the cardio-pulmonary system dependent on age, for normal persons and elderly sportsmen acc. to Strau-zenberg as well as resting O_2 absorption and Q_{O_2} at rest (STPD conditions) dependent on age for a normal person calculated acc. to [48] and O_2 MT patients

was achieved in the arrangement shown above by the use of a flow sensor covering the range from 0.12 to 20 l/s. In addition, the flow chan-

nels were designed with an inner diameter of more than 20 mm in order to keep the flow resistance sufficiently low, even in flow peaks.

1.1.5.6 Determining the lung function parameters

Pneumologists (Petro, Daum) were, as quoted in [17], of the opinion that the oxygen multistep therapy procedures could not bring about a lasting improvement of the parameters of lung function [59]: 'None of these partial functions of respiration can be changed in any way by the exogenous supply of oxygen'. This standpoint was opposed by the author's expectation that, by means of the high-charging of the blood microcirculation in the lung area also, and the lasting improvement in the energetic status (an increase in the performance capacity of the respiratory musculature), a long-term improvement in the parameters of lung function does or can occur. In order to settle this question a pilot study was performed, at first by Dr Gabriele Caspers and finally by us. For this a Spiroton-2 device from the Drägerwerk, Lübeck, FRG, was used, made available by the courtesy of the Erwin Braun Institute of Preventive Medicine, Engelberg, Switzerland. This instrument determines from a single expiratory breath, which can be repeated twice after an adequate interval, the parameters exemplified in the two following cases. The parameters are retrieved from a memory and are evaluated inside the instrument. The results are presented by a plotter as flow and volume/time curves. In this way the following results were documented, showing that *lasting improvements in lung parameters due to oxygen multistep therapy* really can be objectified (see column, right).

In 15 patients from our group we found an increase of 6.5 % in the vital capacity and of 15.4 % in the peak flow (PF) after O₂MT.

1.1.5.7 Determining the resting CO₂ production as a characteristic value of the oxygen utilized by the organism

In order to be able to differentiate the metabolic pathways of the (additionally) absorbed oxygen in the organism, it is also necessary to determine quantitatively the CO₂ emission of the lungs. Figure 23 shows a schematic picture of these pathways. The absorbed oxygen is used for energy production (biological oxidation) in the respiratory chain of the mitochondria of all cells. Part of the energy gained is required for immune processes, detoxification reactions,

Case 1: 24-year-old male patient with functional vegetative complaints. Treatment: two 15 min O₂MT quick procedures

Parameter	before	after O ₂ MT	Difference	
			abso- lute	relative
Peak flow [l·s ⁻¹]	8.21	10.50	+ 2.29	+ 28%
FVC [l]	5.27	6.04	+ 0.77	+ 15%
FEV ₁ [l]	4.28	4.26	- 0.02	0%

Case 2: 54-year-old male patient with obstructive ventilation disorder. Treatment: 36 h 18 day O₂MT procedure

Parameter	before	after O ₂ MT	Difference	
			abso- lute	relative
Peak flow [l·s ⁻¹]	4.68	5.81	+ 1.13	+ 24%
FVC [l]	3.39	3.60	+ 0.21	+ 6%
FEV ₁ [l]	1.87	2.08	+ 0.21	+ 11%

Explanation of the abbreviations:

- Peak flow = maximum expiratory flow
- FVC = forced vital capacity (in maximum expiration)
- FEV₁ = 1-second forced expiratory volume; Tiffeneau test

Dr Gabriele Caspers also produced similarly positive findings with improvement in these and further lung parameters on 171 patients in the Klinik für Naturheilverfahren, Bad Füssing, FRG [60, 400a].

in hormone syntheses and in protein metabolism.

The CO₂ production per unit of time (l·min⁻¹) can be determined by measurement of the absolute CO₂ content of the expiration air.

Information about the *oxygen actually converted* in the organism can thus be obtained by measuring the CO₂ emission. The significance of this parameter is subject to three limitations, however:

For comparison:

basal metabolism relationship youth / age
 $BM_{20\text{years}} = 167 \pm 23 \text{ kJ h}^{-1} \text{ m}^{-2}$
 $BM_{75\text{years}} = 133 \pm 18 \text{ kJ h}^{-1} \text{ m}^{-2} = 1,26 \approx 126\%$
 (normal values of healthy men
 acc. to Du Bois, see Geigy Tables)

After O_2 MT a lasting increase of the resting O_2 -uptake Q_{O_2} to 227% was spirometrically measured in weakened patients, and from measurements of the $P_{O_2\text{-art}}$ and $P_{O_2\text{-ven}}$ at rest a lasting increase of the O_2 transport to the body tissue to roughly 230% (paper no. 333)

For comparison:

in healthy persons of all age groups a mean increase in Q_{O_2} at rest, to only 133% was determined

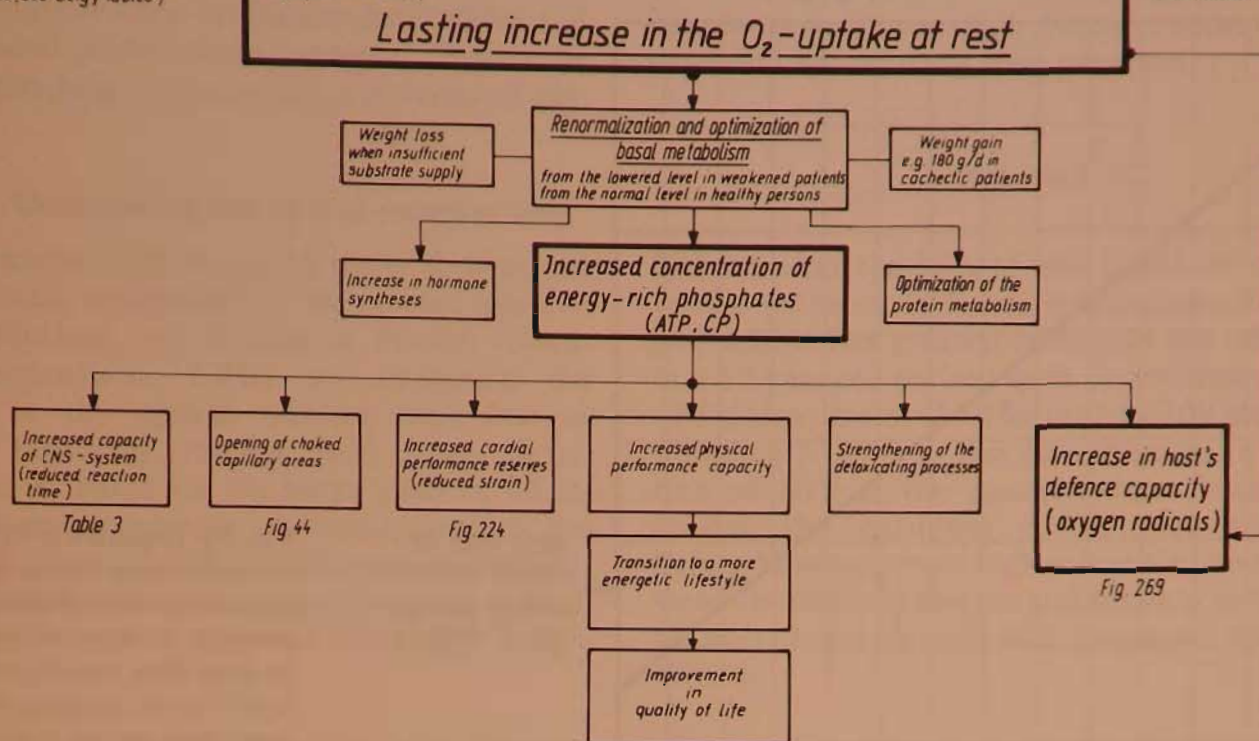


Fig. 23 Where in the organism does this extra absorbed oxygen remain? It follows from spirometric measurements (see appendix) that approx. 50% of the extra oxygen offered after O_2 MT is metabolized to CO_2

1. A not inconsiderable portion of the CO_2 formed is re-used immediately in the organism for syntheses (especially fatty acids), and therefore does not appear externally. It is important to know this for the basal metabolism.
2. In comparison with a certain absorbed and used amount of O_2 , the amount of the CO_2 formed per unit of time is also dependent on the type of nutrients as "fuel". Fatty acids contain less oxygen than glucose, for example; therefore the intensity of metabolism and CO_2 production is reduced at the same O_2 flow. These facts are reflected in the "Respiratory Quotient" (RQ):

$$RQ = \frac{CO_2 \text{ production (ml} \cdot \text{min}^{-1})}{O_2 \text{ uptake (ml} \cdot \text{min}^{-1})}$$

At standard conditions (basal metabolism the RQ is ~ 0.82 , corresponding to a CO_2 production of 250 ml/min and an O_2 uptake

of 300 ml/min. As a rule, RQ increases after O_2 MT (e.g. up to 0.9) and with increasing performance. At about 2/3–3/4 of the maximum performance capacity (physical exertion) RQ reaches a value of 1.0, which corresponds to an exclusive glucose oxidation.

3. In great *physical exertion* and corresponding metabolic acidosis (due to the anaerobically formed lactic acid) the RQ rises to over 1.0 as a result of an over-proportional CO_2 release with only a slightly or not at all increased O_2 uptake. The falling CO_2 partial pressure in the arterial blood indicates that the CO_2 expired comes from the normal blood stock and corresponds to a respiratory compensation (hyperventilation in maximal exertion) for the metabolic acidosis.

This excess CO_2 therefore does not stem from the oxidative metabolism, so that the CO_2 output measured under maximal exertion has only limited meaning.

1.1.5.8 Determining the physical performance capacity

Two series of experiments have been carried out to determine the physical working capacity (PWC) before and after O_2 MT. In the first series (1982/83) we measured the PWC before and

after two 15 min O_2 MT quick procedures using bicycle ergometry with a gradual increase in load, and establishing the PWC_{130} (physical working capacity in watts at a pulse frequency

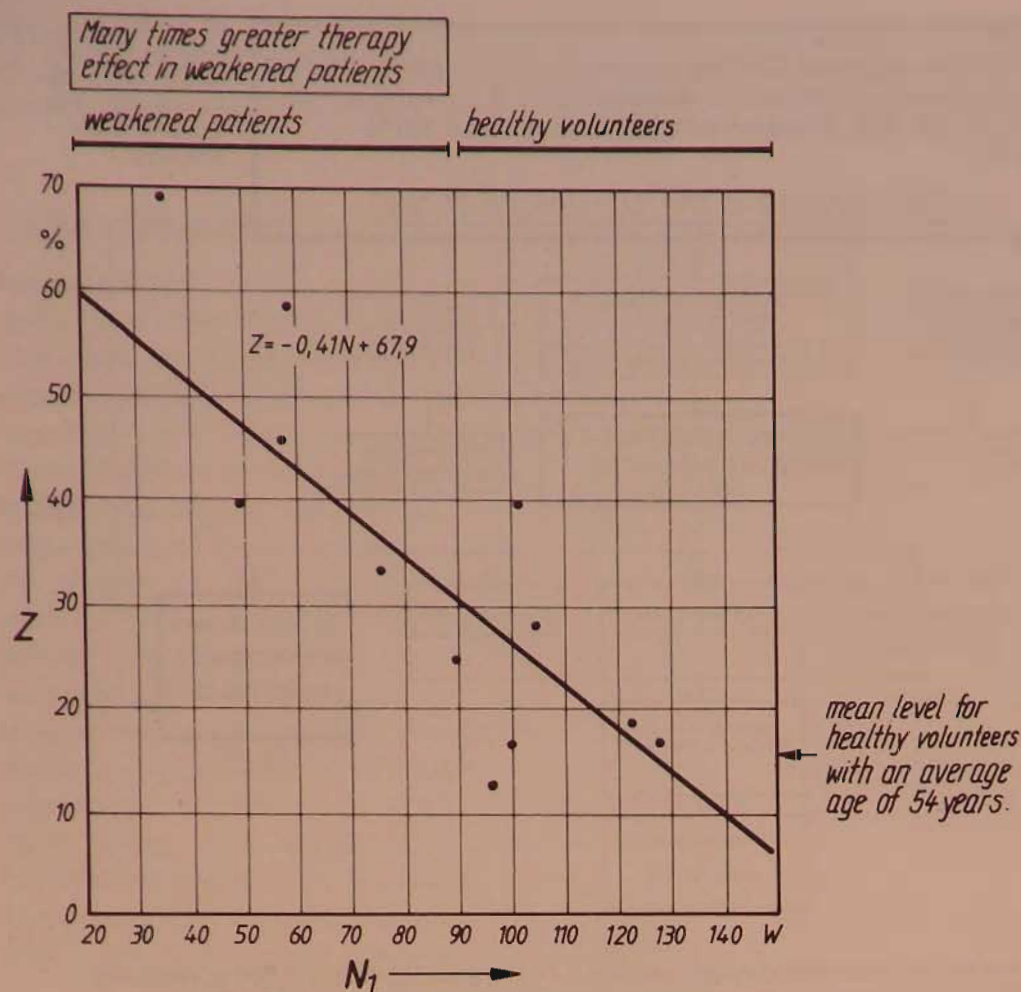


Fig. 24 Ergometric PWC_{130} measurements showing the percentage of increase Z of physical working capacity 14 days after two 15 min O_2MT quick procedures, dependent on the level of performance N_1 before therapy

of 130 per min) in 10 male volunteers in each case, with an average age of 54 years, under conditions of a double-blind study. The PWC_{130} was re-measured 2 weeks after the last quick procedure (lasting effect). It had increased from 115.2 to 134.3 watts, in other words, by 19.1 watts or 17 % (statistically significant at $p < 0.05$). In the control group (with placebo and compressed air) only an insignificant increase of 5 % occurred, as a result of the training effect.

We performed the second series of tests in 1984 with volunteers of both sexes with an average age of 61, before and after the 36 h 18 day O_2MT procedure with administration of Alupent and daily 10 min training (following the O_2MT sessions). The PWC_{130} , which was lower in these older volunteers (91.7 watts before O_2MT) rose to 119.3 watts after this more time-consuming and laborious O_2MT variant, that is, by 27.6 watts or 30 % (statistically significant at $p < 0.001$). The maximal performance capacity was also increased, i.e. in five out of ten individuals one or, in one case, even two further 25 watt steps were achieved.

The blood pressure measured on the highest step of the starting ergometry sank significantly ($p < 0.05$) from 180.6 to 164.4 mmHg, that is, by 16.2 mmHg or 9 % (from 24.1 to 21.9 kPa, i.e. by 2.2 kPa).

The results stemming mainly from the first series with the 15 min O_2MT quick procedure are given in Fig. 24. They confirm again that *the O_2MT effect in weakened patients is many times greater than in healthy persons*. The last part of the book gives an overview of the medicinal consequences of this effect, which is so strong in weakened or ill patients. Even the lesser effect in healthy individuals is of great practical significance, especially for the prevention and prophylaxis of diseases, ailments and complaints. If, for example, it can be seen in healthy individuals that the oxygen status is worsening, the energetic reserves of the organism are falling and the physical performance capacity is dropping, the deterioration of the measured values should be stopped and even reversed, e.g. by means of the O_2MT immunostimulation, by which both the oxygen status and the host's immune defense capacity are improved to such an extent that overt disease and crises do not result. A procedure of this preventive kind should become one of the main characteristics of future medicine. The lasting increase in the physical performance capacity that has become possible is also of interest to persons with normally good health, although it is at a level of only 10 %. Even such moderate gains can be decisive for victory in sports competitions. The author knows of various positive examples of this kind from top-

class sport, with implementation of the 15 min O₂MT quick procedure days or weeks before the competition. Singing, too, is a conversion of physical energies. Experience shows that the lasting improvement in the energetic status and the physical performance capacity seems to be able to give help to singers who, in terms of age,

are approaching the peak of their vocal performance. An increase in the vocal performance (acoustically measurable), a longer preservation of the singing performance capacity during the culmination phase, and better endurance of extended appearances were observed.

1.1.5.9 Determining the optical reaction time

One parameter which can be easily determined using simple equipment is the *optical reaction time*¹. Working on an idea of Fischer (Nordrach-Klausenbach, FRG) we examined the change in the optical reaction time due to oxygen multistep therapy [63]. Every determination is based on the mean value of 20 individual measurements performed within the space of 3 min. In 20 volunteers of both sexes, with a mean age of 60 years, the mean optical reaction time was reduced from 297 ms to

235 ms after the 36 h 15 day O₂MT procedure, i.e. by 44 ms or 16 % (statistically significant at $p < 0.05$). The greatest reduction was observed in a 68-year-old patient with cerebrovascular insufficiency, from 515 (before) to 309 ms (after treatment). Thus in this case there was a reduction of 40 % in the reaction time. In cases involving the existence of extreme tiredness before therapy, even higher levels of reduction were observed. In the control series, a reduction of only 5 ms or 2 % was measured (training effect).

¹ For measurement of the critical fusion frequency and of the information flow to the short-term memory C_k see [62]

Table 3 Optical reaction time in milliseconds (ms) of 20 individuals before and after O₂ multistep therapy (mean values $\pm$ s.e.m. from 20 separate measurements each within 3 min)

No.	Sex		Age years	Diagnosis	before O ₂ MT ms	after O ₂ MT ms	Difference	
	m	f					absolute ms	relative %
1		f	71	chronic CVI	275 $\pm$ 42	260 $\pm$ 52	-15	- 5,5
2	m		55	glaucoma	256 $\pm$ 23	226 $\pm$ 25	-30	-11,7
3	m		52	chronic IHD	245 $\pm$ 46	204 $\pm$ 27	-41	-16,7
4		f	55	migraine	292 $\pm$ 96	215 $\pm$ 27	-77	-26,4
5		f	52	glaucoma	295 $\pm$ 56	298 $\pm$ 82	+3	+ 1,0
6	m		76	ageing prophylaxis	209 $\pm$ 56	199 $\pm$ 17	-10	- 4,8
7	m		45	solvent exposition	202 $\pm$ 18	185 $\pm$ 23	-17	- 8,4
8	m		52	chronic CVI	253 $\pm$ 76	231 $\pm$ 33	-22	- 8,7
9	m		71	chronic CVI	282 $\pm$ 82	258 $\pm$ 46	-24	- 8,5
10		f	63	chronic CVI	276 $\pm$ 46	218 $\pm$ 21	-58	-21,0
11	m		68	chronic CVI	515 $\pm$ 139	309 $\pm$ 58	-206	-40,0
				chronic IHD				
12	m		80	chronic heart failure	290 $\pm$ 113	212 $\pm$ 22	-78	-26,9
13	m		48	chronic CVI	295 $\pm$ 141	224 $\pm$ 22	-71	-24,1
14		f	63	chronic IHD	259 $\pm$ 43	208 $\pm$ 30	-51	-19,7
15	m		64	borderline hyperthyreosis	246 $\pm$ 62	228 $\pm$ 47	-18	- 7,3
16	m		57	chronic CVI	375 $\pm$ 208	320 $\pm$ 115	-55	-14,7
17	m		71	DAH	248 $\pm$ 52	235 $\pm$ 22	-13	- 5,2
18		f	40	chronic CVI	239 $\pm$ 35	204 $\pm$ 31	-35	-14,6
19		f	62	chronic CVI	302 $\pm$ 64	256 $\pm$ 26	-46	-15,2
				chronic IHD				
20	m		55	diabetes mell. chronic IHD	228 $\pm$ 27	220 $\pm$ 30	- 8	- 3,5
20	13	7						
x $\pm$ s					279,1 $\pm$ 85,0	235,5 $\pm$ 44,5	-43,6	-15,6

The discovered reduction in the optical reaction time should be a great help to the following group of people:

1. airline pilots;
2. older car-drivers approaching the limit of their fitness to drive;
3. car-drivers who are easily fatigued or who have to undertake long journeys;
4. car-drivers with circulatory lability;
5. racing drivers.

It is known that the continually repeated *elementary process in driving a car* consists in the visual perception of the current road and traffic conditions which – delayed by the “optical response time” – triggers meaningful control reactions (steering processes, braking and accelerating processes etc.). The shorter the individual, momentarily existing optical response time, the more able the driver is to avoid critical traffic situations and accidents, or to minimize the danger of human life as well as material damage in occurring accidents.

1.1.6 Establishing and influencing the “biological” age

In order to establish the “biological” age, the vital parameters of test subjects are determined using a procedure inaugurated by Pögelt and Roth and further developed by Ries [64] and Pöthig [65, 66], showing significant age-dependent changes. The individual results in each case are mathematically processed in the “Geromat device” (producer: Halberstadt District Hospital, GDR), and the result presented as the biological index. Six different parameters are included in the test: the measurement of the optical reaction time to a light stimulus and a

pointer deflection; the measurement of the acoustic reaction time to a tone of a certain frequency and intensity; the recording of visual-motoric capacities; tapping test; search test in accordance with Millner etc.

In a pilot study with this device and other given methods, the following results were obtained in volunteers who had ensured a *good O₂ status by means of O₂MT almost uninterruptedly over a period of 15 years*, showing a significant reduction in the “biological” age by oxygen multistep therapy:

No.	Sex	Chronological age (yr)	Resting PO_{2-art} (mmHg)		Method of determination (vital parameters)	Biological age (yr)
			measured	expected		
1	m	79	69 ($\eta \approx 22\%$)	84 ($\eta \approx 50\%$)	Ries-Pöthig Geromat system (> 6 parameters)	64
					Quality of the vascular system	50 $Q = 0.0176$
					PO_{2-art} at rest; measured vs. expected	40
					Skin elasticity	55
2	f	70	72 ($\eta \approx 23\%$)	82 ($\eta \approx 40\%$)	Ries-Pöthig Geromat system (> 6 parameters)	47
					Quality of the vascular system	40 $Q = 0.021$
					PO_{2-art} at rest; measured vs. expected	41
					Skin elasticity	45

A further factor which could in future contribute significantly to the determining of the biological age is the determining of the vascular

ment of the intravascular PO_2 after the release of a previous tourniquet. This method, which is discussed below in Paragraph 3.4.4 (Fig. 3.12), also has the advantage of being

vasive and routinely applicable. This easily attainable parameter can be seen as generally diagnostically interesting, as changes in the

vascular system due to events of the most varied kind (e.g. O₂MT) are reflected in it.

We are still far from a standardization of the methodology of the biological age [67, 110].

1.1.7 Methods of assessing the blood microcirculation

The quantitative or even just qualitative assessment of the blood microcirculation is of very great informative value. Examples are:

1. Direct determination of the increase in the blood microcirculation in the tissues of the organism by means of triggering the capillary switching mechanism of the oxygen multistep therapy.
2. Recognition of placenta insufficiencies and their elimination using O₂MT.
3. Recognition of the time point of the selective vascular occlusion in the cancer tissues after cancer multistep therapy (CMT).
4. Recognition and elimination of peripheral circulatory disorders, etc.

A simple way to assess the blood microcirculation in tissue near the body surface (maximum depth approximately 2 mm) is the method of *laser Doppler flowmetry* [68]. One instrument suitable for this is the Periflux made by Perimed, Sweden. The nail fold of the 3rd or 4th finger is a suitable site to detect all the flow

changes [69]. Exactly the same point of measurement can be easily re-found by micro-marking, the temperature can be measured using a thermistor and can be kept constant by a thermostat. This method is well suited to document directly the increase in the blood microcirculation due to the triggering of the capillary switching mechanism of the O₂MT. This technique can also be used to determine the increase in the blood microcirculation during physical exertion and under medication with sympathicomimetics, such as Alupent.

A further way to assess the blood microcirculation in tissue which can extend to approximately 20 mm under the body surface is the method of *ultrasound Doppler flowmetry*. Here a small portion of ultrasound radiation is scattered or reflected by the disturbed blood corpuscles and thus, in accordance with the size and orientation of speed, Doppler-shifted. With increasing frequency and hence decreasing wavelength λ the back-scattered portion increases and obeys the $\frac{1}{\lambda^4}$ dependency (Ra-

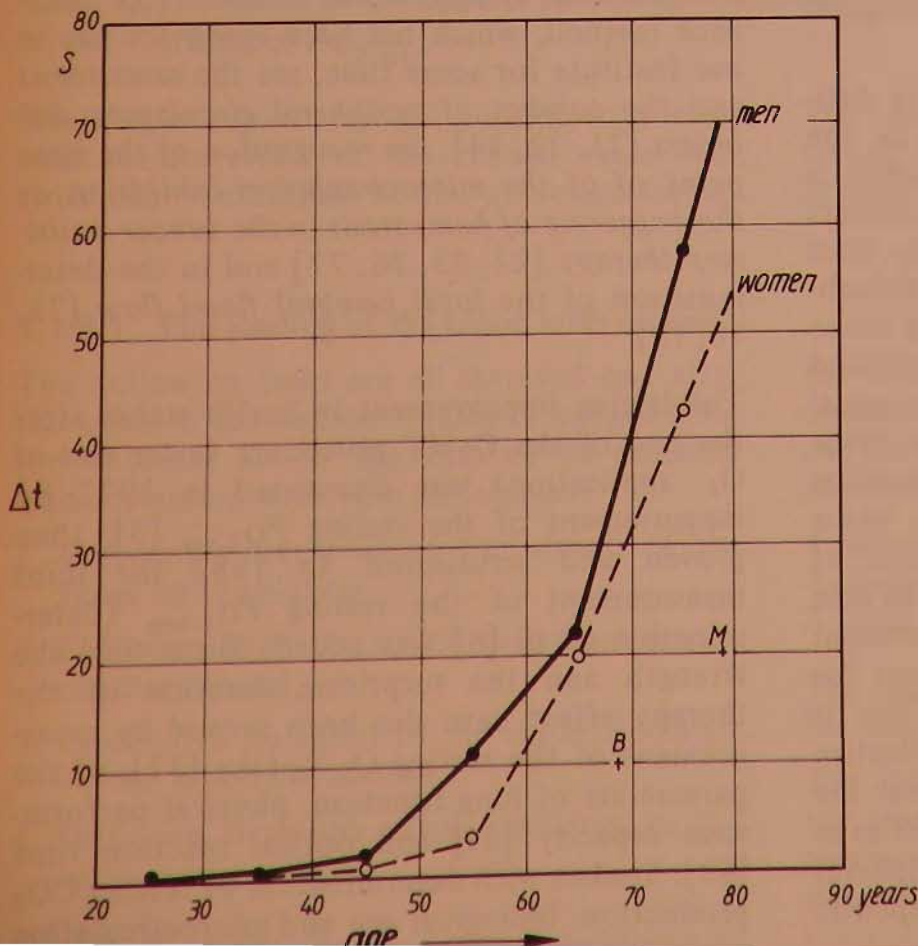


Fig. 25 Smoothing time Δt for a skinfold on the back of the hand caused by pulling up, dependent on age. Δt as a marker¹ of skin elasticity

¹ Mean over many preceeding months

leigh's law), if the condition that $d \leq \lambda$ (d = particle diameter) is fulfilled. The Doppler frequency shift Δf of the wave scattered back by the moved particles is proportional to the transmitter frequency f_0 and the particle velocity v , projected onto the transmission or receiver direction:

$$\Delta f = f_0 \cdot \frac{2v}{c - v}, \text{ with } c = \text{speed of sound}$$

The velocity range of the blood corpuscles relevant for the microcirculation lies between 5 and 0.5 mm/s. Using an ultrasound instrument designed in our Institute for this task, an US frequency of 7.5 MHz is applied. The value of Δf is therefore only a few Hz. (By comparison, with the laser Doppler flowmeter, working with light, the value of Δf is 1–2 kHz.)

The speed orientation of the blood corpuscles in the area of small vessels is completely isotropic, so a Doppler frequency spectrum of the blood velocities of < 5 mm/s occurs symmetrically with the transmission frequency, by contrast to the asymmetric Doppler spectrum of the flowing blood in larger vessels.

Our apparatus uses the *impulse Doppler process*. Firstly it enables a critical intensity not to be crossed despite high impulse energies and, secondly, a *selection in depth* is possible.

The electronic processing of the back-scattered signal with subsequent Fourier analysis makes possible the assessment of a narrow range of velocity. With the developed multi-element transducer, analysable signals up to penetration depths of almost 2.5 cm can be gained.

An exact interpretation of the results is difficult and requires great experience, as the measured value, the amplitude of which is determined by the amount of moving scatterers and the Doppler frequency by the velocity, does not allow us to distinguish between the disturbing blood corpuscles and other moving tissue parts. It is particularly necessary in this method to distinguish the required measurement signal from those signals which occur due to tissue movement in the pulse rhythm. It should be stated here, however, that even these tissue movements represent an indirect measure of tissue circulation. This method will not be able to claim to be a reliable, absolute measurement process. It should, however, be sufficient for a qualitative relative measurement. Thus it could help in the recognition of the selective vascular occlusion in the cancer tissue near the surface in cancer multistep therapy, as well as in the recognition of the elimination of peripheral circulatory disorders by means of therapeutic

A frequently used way to assess the blood microcirculation in tissue which can be at any depth beneath the body surface, is the ^{133}Xe clearance method. The ^{133}Xe isotope of the heavy inert rare gas is almost ideally suited for use in humans due to its short half-life of 5.27 days and its γ -radiation energy of 81 keV, as well as its relative frequency of 27% [70]. Depending on the aim envisaged, the radioactive isotope is added to the circulation, either in gas form via the lungs, or dissolved in physiological sodium chloride solution via the vascular system, usually on the arterial side. The clearance, normally measured with highly accurate and directionally sensitive γ -scintillation counters in the target area, correlates with the tissue blood flow, hence, with the microcirculation [72].

In the view of Reference [70] and the fact that the author set up the laboratory for nuclear medicine of the Medical Academy of Dresden in 1964, and from the knowledge of the work [72] from the year 1967, it was obvious that the ^{133}Xe clearance method should be used to test whether it is possible to ameliorate an existing placental insufficiency (disturbed fetomaternal-placental relationship) by means of the oxygen multistep therapy. The impulse for experiments along these lines resulted from a discussion with Kyank. Several gynecological study groups followed from this stimulus, and we learned of positive results [73].

Further areas of application of the ^{133}Xe clearance method, which has been ready for use in our Institute for some time, are the *assessment and the combat of peripheral circulatory disorders* [71, 72, 74], *the recognition of the time point of of the microcirculation inhibition or the triggering of hemostasis in the cancer multistep therapy* [22, 23, 76, 77] and in the determination of the *local cerebral blood flow* [75, 78, 79].

The lasting improvement in health status after the end of the O_2MT procedure (after end of O_2 application) was discovered in 1977 by measurement of the resting $P_{\text{O}_2\text{-art}}$ [3], then proven and scrutinized. In 1982 the joint measurement of the resting $P_{\text{O}_2\text{-ven}}$ (determination of η) [6] was added. Since then the strength and the surprising duration of the therapy effect have also been proved by measurement of the resting O_2 uptake [37], of the parameters of lung function, physical performance capacity [61] and optical reaction time [63]. Studies with determination of resting CO_2 production, biological age and microcirculation are coming along well.

Proof of the unexpectedly long duration of the therapy effect is provided by ever more parameters in ever more medical institutes. Respected clinics have set up studies with the simultaneous measurement of a number of parameters in a large number of weakened patients in need of therapy. It is therefore only a matter of time before it is generally recognized and acknowledged that, *through the discovery and use of the capillary switching process of the blood microcirculation, both medicine and health services have been given a new aid of a universality and efficacy hardly observed hitherto*. The special feature of this aid is primarily that it significantly increases the energy reserves of the (weakened) human organism, long-term and non-invasively.

The author was very much helped in his decision to change from physical to medical research in 1960 by the close, cooperative relations with his friend Prof. Dr med. Bernhard Sprung, the head of the Surgical Clinic of the Medical Academy of Dresden. Due to his premature death, we lost our clinical partner. Since this tragic event we have had to limit ourselves for very many years to methodological development. Being without ambitious clinical partners, we looked for new solutions to important medical tasks on the basis of a physical way of thinking and also the medical knowledge obtained in 52 semesters of research study. We

were supported by the doctors in our Institute and by numerous physicians, biochemists, biologists, rheologists and immunologists all over the world. What followed forms the contents of this book. Time and time again, however, we felt the painful absence of the great, highly recognized clinical partner at our side. Despite various appeals, for many years we could find no suitable clinics prepared to repeat and extend the results obtained in our treatment series, *using large numbers of suitable patients*, and then to report on their results. In this situation, the author is very grateful to the Minister of the Health Service of the GDR, Prof. Dr med. Ludwig Mecklinger, for some time ago allowing and encouraging the establishment of an external *branch of our Institute* at the nearby Weisser Hirsch Clinic (director: Dr med. Heinz Langer) *for treatments with all variants of the oxygen multistep therapy*. The above-mentioned fact that respected clinics in contact with us (avoidance of methodological shortcomings) have this year set up comprehensive, well planned studies, also justifies the expectation of an early breakthrough of the oxygen multistep therapy to form a part of academically recognized and taught medicine.

In the following paragraphs we will discuss the processes, influences and findings of which is necessary to have knowledge for the implantation of the O₂MT procedures.

1.1.8 The effect of the cellular switching mechanism of the microcirculation in the lung; effects of $P_{O_2\text{-art}}$

The lung occupies a special position with reference to the effect of the cellular vessel wall switching mechanism of the microcirculation.

This mechanism leads here to changes in the resting $P_{O_2\text{-art}}$ and hence to changes in the O₂ saturation of the blood.

1.1.8.1 The loading of the blood with oxygen

The following links are all involved one after the other in the transport chain of oxygen from the external air to the sites of its chemical transformation in cellular metabolism:

1. Convective transport to the alveoli of the lungs by ventilation;
2. Diffusion from the alveoli to the pulmonary capillary blood;
3. Convective transport to the tissue capillaries via the blood circulation;
4. Diffusion from the tissue capillaries to the surrounding cells.

the O₂MT are in links 2 and 4. The following are factors influencing the level of the arterial oxygen partial pressure and thereby the strength of O₂ saturation of the blood:

1. alveolar ventilation V_A ;
2. pulmonary blood flow (perfusion) BF;
3. lung diffusion capacity D_L .

The quotients V_A/BF and D_L/BF are decisive for lung performance.

The individual red blood cells migrate through the lung capillaries with the blood flow. During this passage the red blood cell, as Fig. 26 shows, is in diffusion contact with the alveolar space

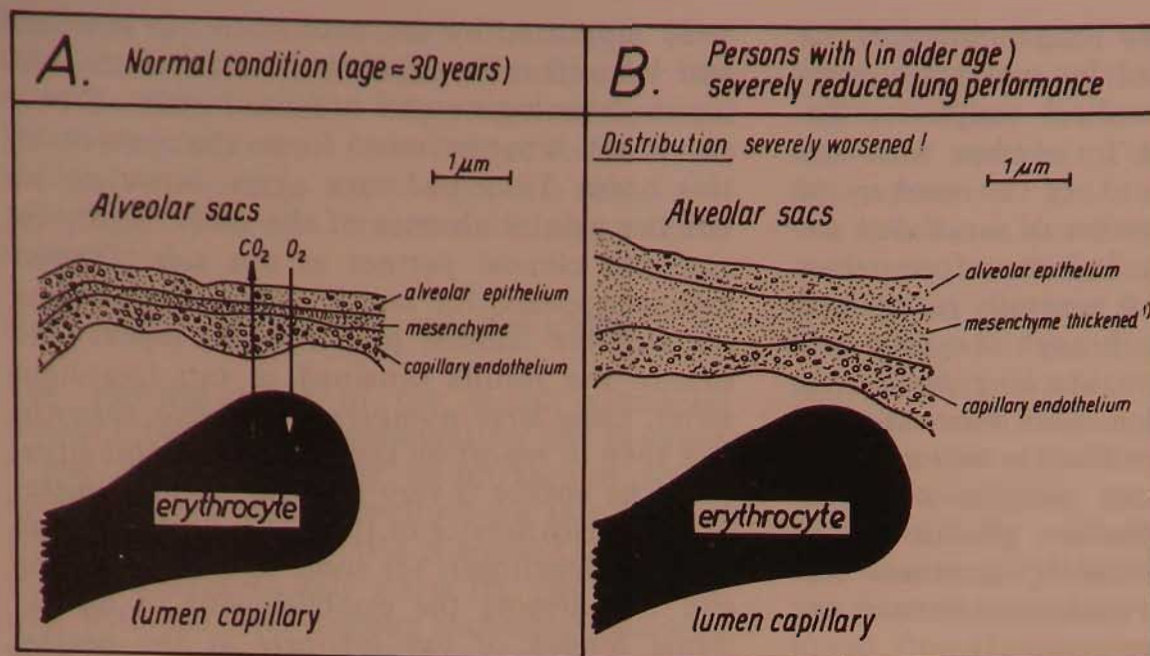


Fig. 26 Diffusion paths for O_2 and CO_2 in the exchange of gases in the lungs (see also [81], Table 8)

¹ Diffusion path enlarged (highly reactive layer). Swelling of capillary endothelium. Narrowing of capillaries. Simultaneous strong increase in ventilatory inhomogeneity

This contact time is, however, usually sufficient – as seen in Fig. 27 – to bring the oxygen partial pressure in the blood into alignment with that in the alveolar space. It should be recognized, however, that a worsening of the O_2 diffusion conditions (e.g. due to reduction of the microcirculation, that is, of the perfusion) and of the pulmonary functional inhomogeneities [80] compared to the norm, must immediately lead to a reduction in the $P_{\text{O}_2\text{-art}}$.

The contact time is reduced during physical exertion, which can lead to smaller O_2 saturation of the individual red blood cell. However, this subsaturation is normally more than compensated for by the increase in perfusion through the lung capillaries which occurs during

physical exertion, and the increase in the P_{O_2} in the alveolar space of the lung, resulting from the increase in the respiratory minute volume (RMV). The result of this is the important fact that the $P_{\text{O}_2\text{-art}}$ increases during physical exertion. In addition to this, there is an increase in the mitochondrial metabolism in the cells of participating organs when extreme physical exertion is regularly undergone. This “training effect” improves O_2 utilization in these organs for limited lengths of time. The effects have already been successfully used in medicine and natural healing (strength-demanding activities, sport etc.) for generations [9–12].

Under the conditions of O_2MT the increased lung circulation which occurs during physical

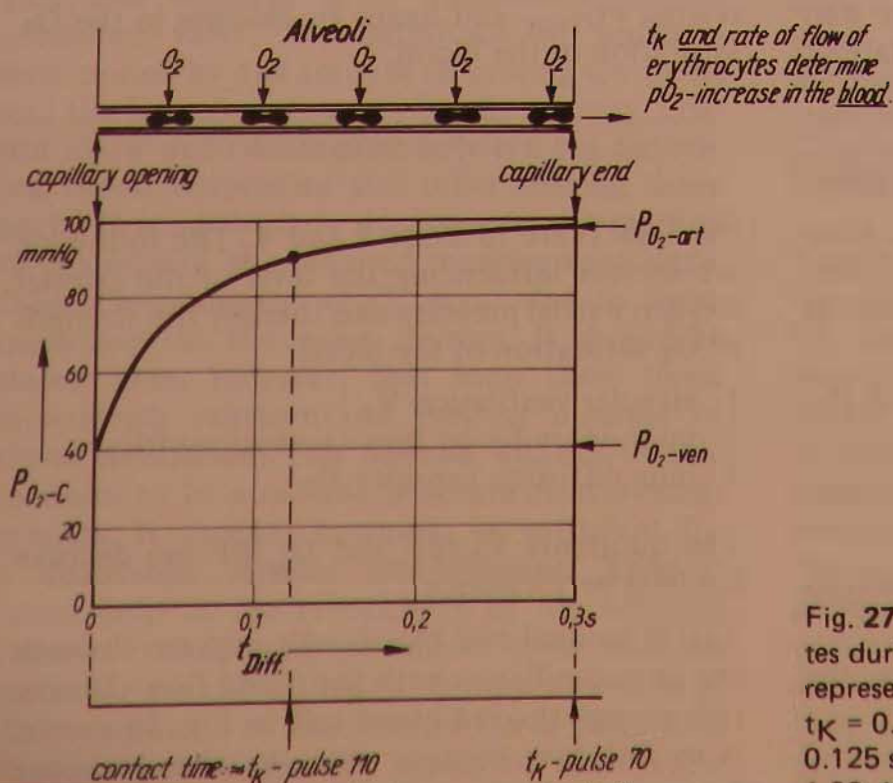


Fig. 27 Increase in O_2 partial pressure in erythrocytes during passage through the lung capillaries, represented for the diffusion contact times [32] $t_K = 0.3$ s (resting conditions, pulse 70) and 0.125 s (strain conditions, pulse 110); $1 \text{ mmHg} = 133.322 \text{ Pa}$

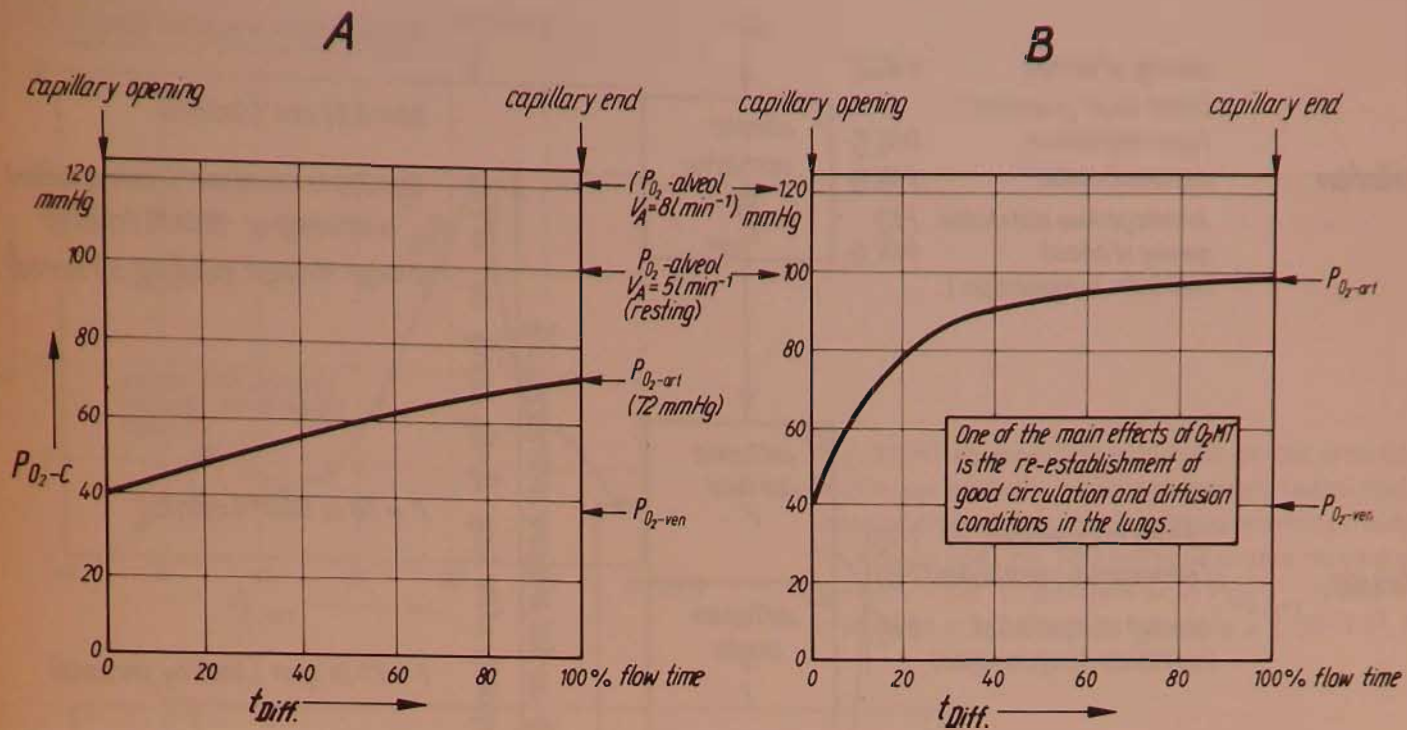


Fig. 28 Increase in O_2 partial pressure in the blood during the passage through the lung capillaries, represented for a 70-yr-old individual with reduced arterial resting PO_2 (A) as expected, and for a 70-yr-old individual with arterial resting PO_2 (B) lastingly raised by means of the O_2 MT by 26 mmHg above the expected level, to 38 mmHg. $1 \text{ mmHg} = 1.33 \cdot 10^2 \text{ Pa}$

exertion brings about a great increase in the flow rate of red blood cells virtually saturated with O_2 , despite the shortened contact time. The desired augmentation of the O_2 offer then occurs for the whole organism.

Just how much the O_2 saturation of the blood in the flow through the lung capillaries is worsened with the reduction in cardiopulmonary performance at an age of, e.g. 70 years, can be seen from diagram A in Fig. 28. The course of the curve emphasizes to what extent the circulation and diffusion relationships in the lung belong to the target area of therapy, when we want to ameliorate or eliminate the reduction in cardiopulmonary performance with advancing age. Diagram B in Fig. 28 gives an example of the effects of the O_2 MT procedure. It shows that the relationships in the lung system can often be regenerated, even in older age, to a degree previously hardly believed possible.

The interrelationships of the factors decisive for the $PO_{2\text{-art}}$ and reactivity of the lung-heart system are shown in Fig. 29. In particular, the couplings and feed-backs existing between the

various elements have been drawn in here. The triggering factor of the reactivity can either lie predominantly in the lung or in the cardiovascular system, or together in both areas. The cellular switching mechanism of the micro-circulation, which lastingly closes, or re-opens the capillaries in the diffusion-perfusion area of the lung, is primarily the main contributor to reactivity. Depending on the type of the triggering factor or of the regulatory mechanism, the reactivity has either a small (τ_1) or a large (τ_2) time constant. We must make a fundamental distinction between degenerating influences (—) which decrease the $PO_{2\text{-art}}$, and regenerating influences (+) which increase the $PO_{2\text{-art}}$.

Figure 30 shows a typical example of PO_2 reactivity with a small time constant. Another example of arterial PO_2 reactivity with a small time constant is the reduction of almost 10 mmHg (1.3 kPa) in the $PO_{2\text{-art}}$ due to a dose of 1.6 mg nitroglycerol. Among others, Fig. 17 above is an example of arterial PO_2 reactivity with a large time constant.

1.1.8.2 The reduction in the $PO_{2\text{-art}}$ due to age and stressful influences

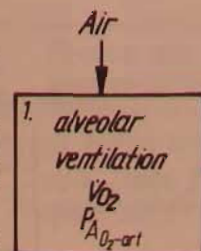
In a non-selected group of patients the $PO_{2\text{-art}}$ values vary over a wide range. Figure 31 gives information about the distribution of measured

There is a very pronounced and characteristic dependence of the mean $PO_{2\text{-art}}$ on age, as can be seen in Fig. 32. It is natural that the reduction in $PO_{2\text{-art}}$ with age greatly contributes to

A. Ventilation

closing of alveoli
(funct. shunt proportion)
hyperventilation
hypoventilation
inhomogenous distribution
opening of alveoli
(contributes to regeneration)

$(-)\tau_1, \tau_2$
 $(+)\tau_1, \tau_2$
 $(-)\tau_1, \tau_2$
 $(-)\tau_2$
 $(+)\tau_1, \tau_2$



$$V_A \approx 4.5 \text{ l} \cdot \text{min}^{-1} (\text{adults})$$

$$\dot{V}_{O_2} \approx 250 \text{ to } 300 \text{ ml} \cdot \text{min}^{-1} (\text{resting, adult})$$

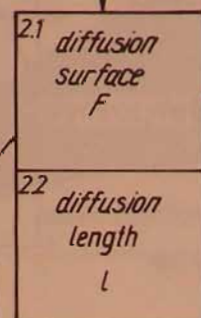
$$P_{A_{O_2}} \approx 100 \text{ mmHg or } 13.3 \text{ kPa} (\text{resting})$$

(+ change through speaking, strain etc.)

B. Diffusion

closing of capillaries
[inhomogenous distribution]
opening of capillaries
(contributes to regeneration)

$(-)\tau_2$
 $(-)\tau_2$
 $(+)\tau_2$



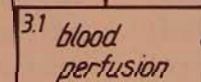
$$F \approx 50 \text{ to } 80 \text{ m}^2 (\text{adults})$$

$$L \approx 2.5 \text{ to } 3 \mu\text{m} (\text{healthy persons})$$

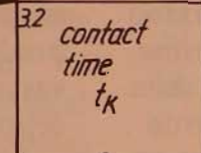
C. Perfusion

shunt perfusion
dependent on the
body's position

$(-)\tau_2$
 τ_1

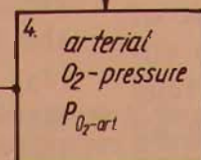
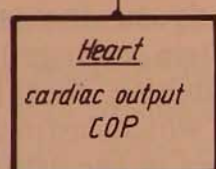


$$Q \approx 0.98 \text{ COP} (\text{healthy persons})$$



$$t_K \approx 0.3 \text{ s} (\text{healthy persons})$$

$$\text{COP} \approx 6 \text{ l} \cdot \text{min}^{-1} (\text{resting, adults})$$

D. Parameter

$$P_{O_2-art} \approx 100 \text{ to } 70 \text{ mmHg} (\text{healthy persons})$$

$$13.3 \text{ to } 9.3 \text{ kPa}$$

Fig. 29 The factors of the lung-heart system determining the arterial O_2 partial pressure and reactivity [82].
K = diffusion conductivity. Time constants of reactivity: τ_1 = a few seconds (sphincters), τ_2 = 15 min to several hours

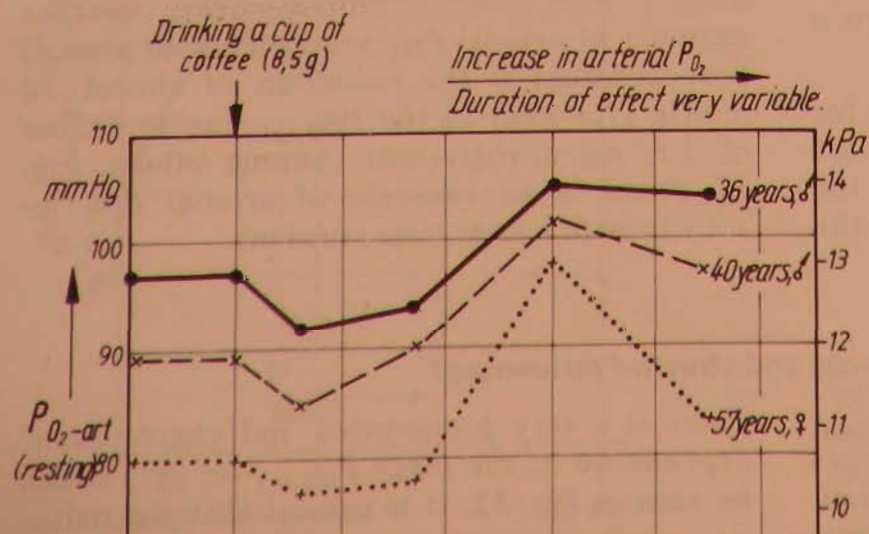


Fig. 30 Influence of drinking a cup of coffee (8.5 g) on the momentary level of the



Figure 1

Figure 1 shows the results of the experiment. The data indicates that the system is capable of performing the task with a high degree of accuracy. The results are consistent with the theoretical predictions and demonstrate the effectiveness of the proposed method.



Figure 2

The graph illustrates the relationship between the variables X and Y. The curve shows that as X increases, Y also increases, but the rate of increase slows down as X approaches a certain value. This behavior is characteristic of a saturation curve, which is often observed in systems where the output is limited by the input or the system's capacity.

The data points for the graph were collected from a series of experiments conducted under controlled conditions. The results show a clear trend that supports the hypothesis that the system's performance is directly related to the input variable X. The graph provides a visual representation of this relationship, allowing for a more intuitive understanding of the system's behavior.

The graph also highlights the importance of the parameter Y in determining the system's output. The curve shows that Y has a significant impact on the system's performance, and its value must be carefully controlled to achieve the desired results. The graph serves as a valuable tool for analyzing the system's behavior and for identifying the factors that influence its performance.

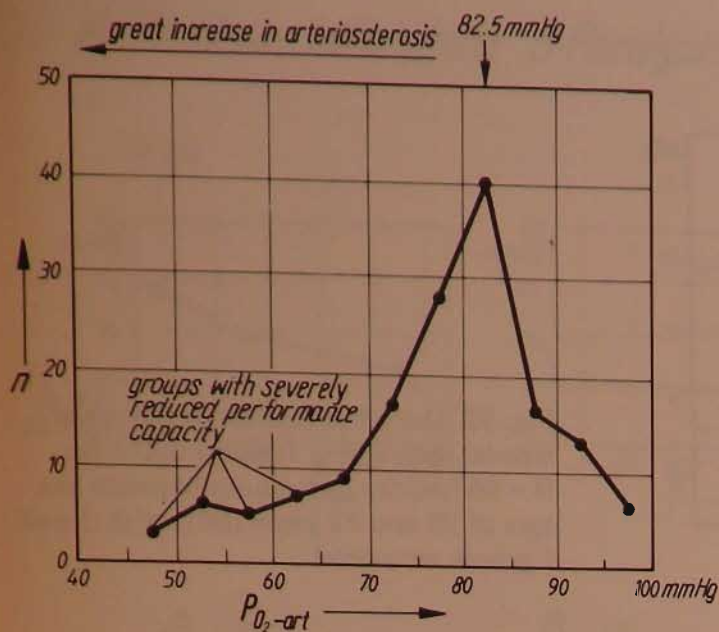


Fig. 31 Frequency distribution of the arterial P_{O_2} in clinical patients of all age groups (admitted under various diagnoses) acc. to measurements made by H. Krauss [84] on 150 persons under resting conditions. n = No. of persons with $P_{O_2\text{-art}}$ levels in the interval $x \pm 2.5$ mmHg. $1 \text{ mmHg} = 1.33 \cdot 10^2 \text{ Pa}$

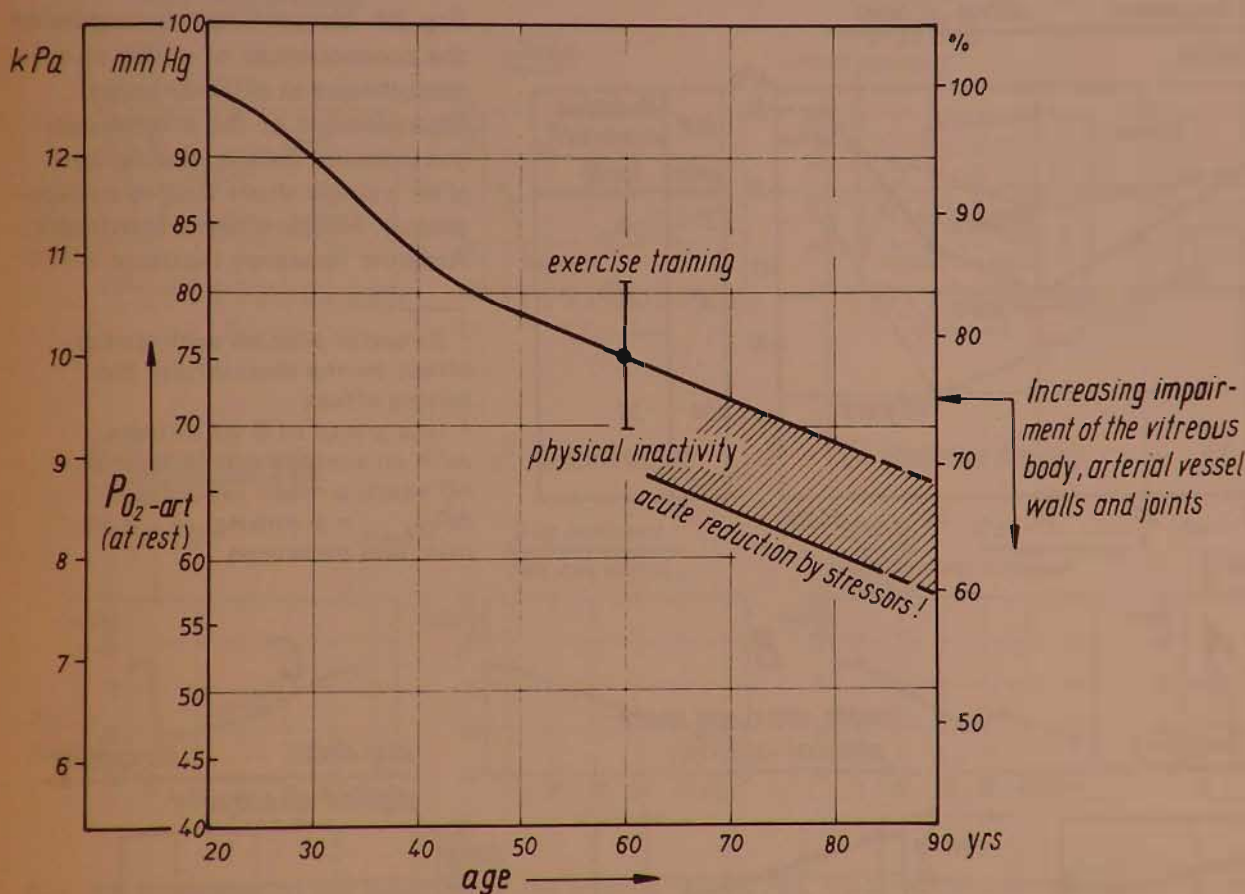


Fig. 32 Average dependence of the arterial oxygen partial pressure $P_{O_2\text{-art}}$, at rest, on age of healthy individuals from the working population, according to Loew and Thews [85]. The age-dependent decline of the resting $P_{O_2\text{-art}}$, which effects a relatively small reduction in the blood, particularly affects tissues that are supplied by direct arterial diffusion (Q_{O_2}). The resting $P_{O_2\text{-art}}$ is a characteristic for the ability of the lung system to take up oxygen (functional state, degeneration, regeneration)

the ageing of the human organism, in particular due to the decline in the arterial diffusion Q_{O_2} . Until our discovery in 1977 [3], this reduction was held to be a physiological regularity hanging over human life with fateful harshness. It was therefore very surprising for us and for others when experimental findings showed that it was usually possible, by means of an oxygen multistep procedure, to raise a reduced arterial P_{O_2} lastingly to levels which existed in the best

The age dependency curve refers to mean values and healthy subjects. In reality, however, we must remember that levels very much lower than those in the curve occur temporarily when a minimum in the circadian cycle is superimposed on the $P_{O_2\text{-art}}$ minima caused by stressful influences (risk factors). Examples of $P_{O_2\text{-art}}$ changes within the circadian rhythm can be seen in Fig. 33.

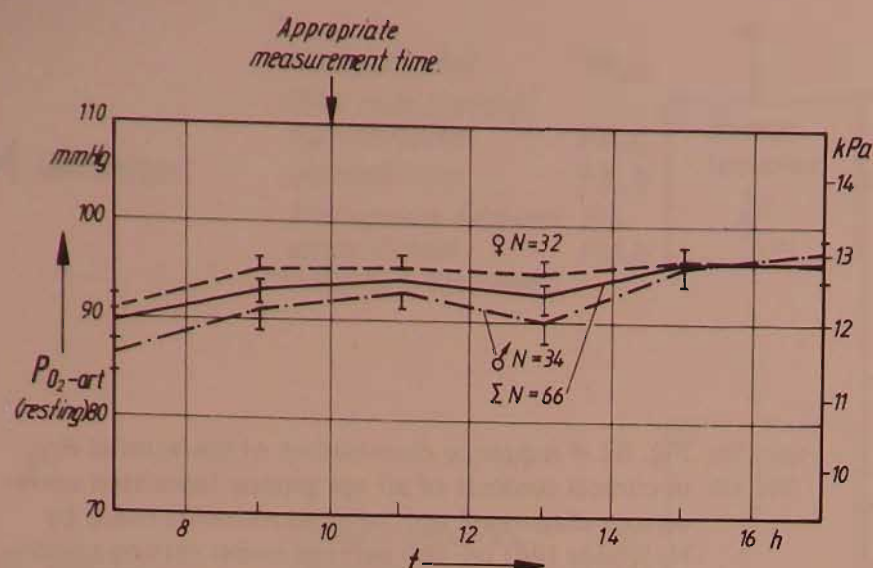


Fig. 33 Daily fluctuation in the mean arterial resting PO_2 (mean $\pm$ S.D.) for $N = 66$ healthy individuals between the ages of 25 and 72 years [86], with δ and φ groups separated

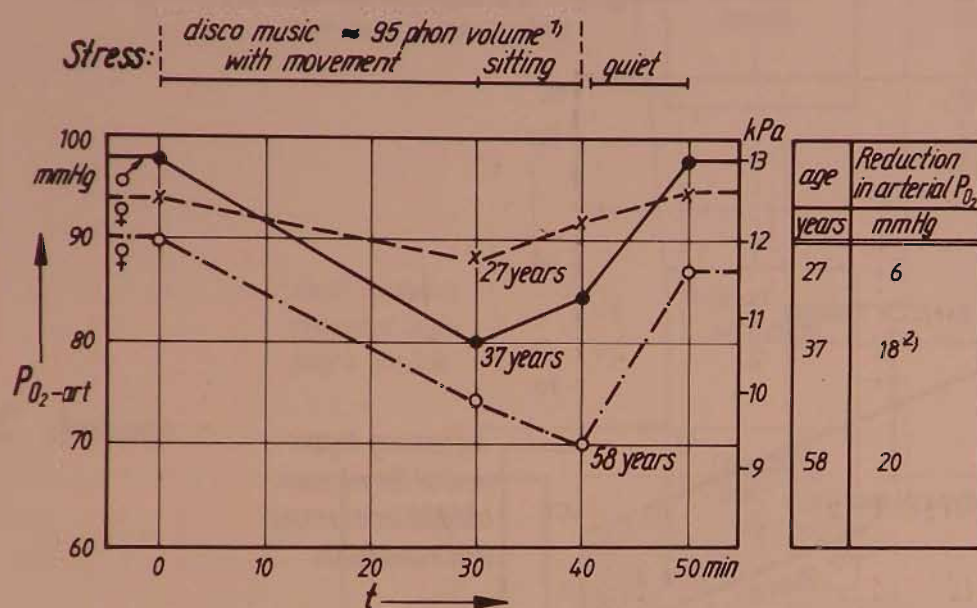


Fig. 34 Measurement examples of the consequences of a visit to a discotheque at different ages. Measurement of the arterial oxygen pressure before, during and after a single short visit to a discotheque. Measurement: Manfred v. Ardenne Research Institute

¹ Stressful process with direct effect on the circulation. No lasting effect

² In a group of 8 volunteers with an average age of approx. 40 years, a mean reduction $\Delta PO_{2-art} = 8$ mmHg, at $t = 30$ min, was measured

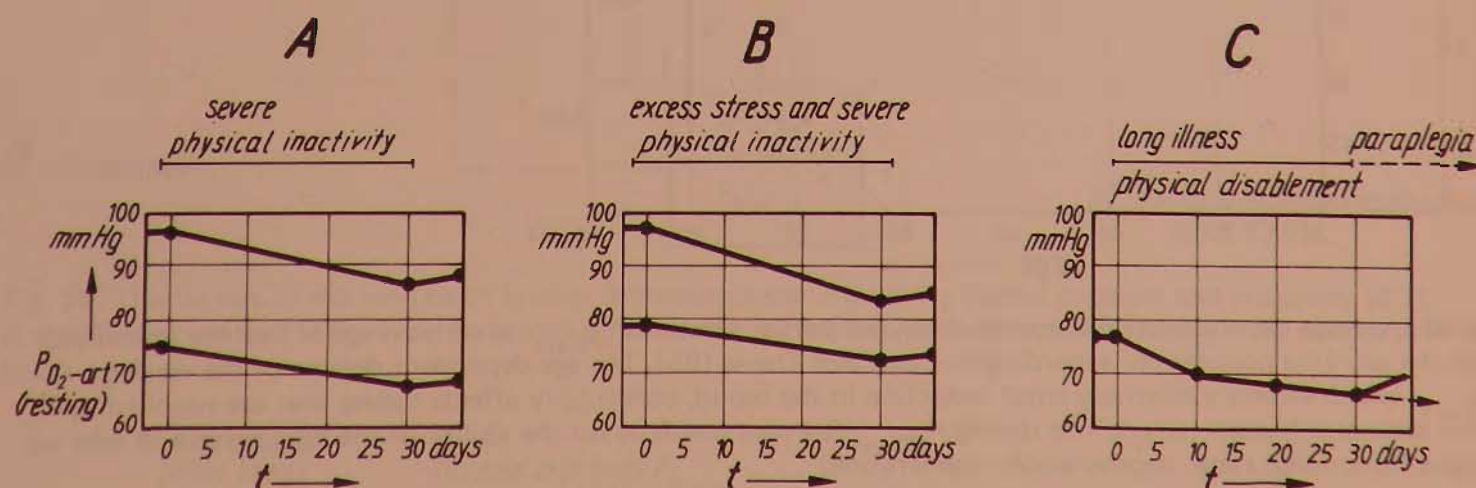


Fig. 35 The reduction in the arterial resting PO_2 by various debilitating effects on the lung-heart system: physical inactivity (A), excess of stress and physical inactivity (B), long illness, physical disablement and paralysis (C)

1.1.8.3 The reduction in the PO_{2-art} due to stressful influences

Special investigations were carried out into the important question of the strength and temporal course of the reductions in the PO_{2-art} due to stressful influences [20, 21]. In doing this it is necessary, as already mentioned, to

distinguish between reactions with small and large time constants. One example in which the depression in the PO_{2-art} forms immediately, i.e. during the action of the stressor, is noise strain, as documented in Fig. 34. The

A Paralysis. Initial phase B Paralysis. Advanced phase

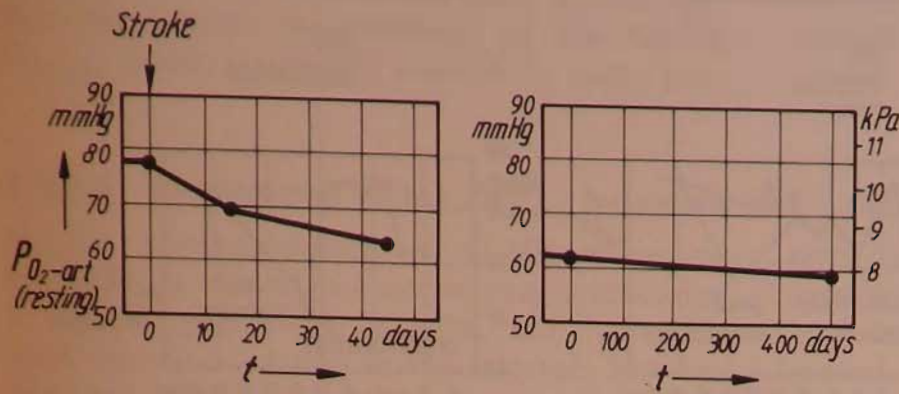


Fig. 36 Examples of the lowering of the arterial resting P_{O_2} by paralysis

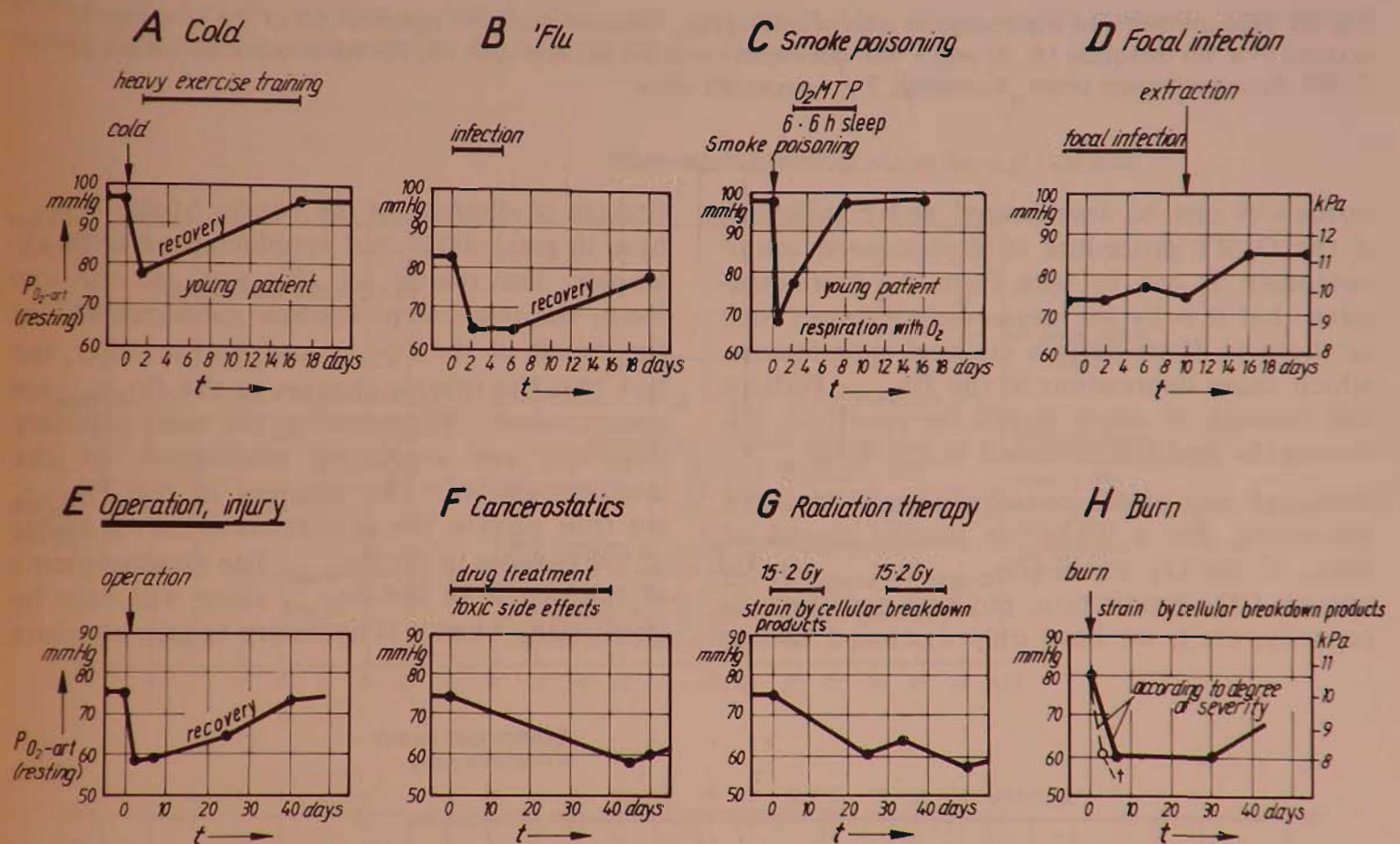


Fig. 37 Examples of the lowering of the arterial resting P_{O_2} by stressful processes of infectious, toxic, and quasi-toxic kind

lung-heart system reacts with a large time constant to most of the other stressful influences which we examined. It can therefore be assumed that the cellular vessel wall switching mechanism is decisive here.

One of the worst stressful influences of our time is the increasing lack of exercise in the modern lifestyle in industrialized states [87]. It is therefore no coincidence that *leisure sport in all its varieties* has become so widespread since the appearance in 1881 of Ferdinand Hartwich's pioneering, rousing work [88]. This development is a sign that a healthy instinct leads us to do what is right, even when

there are no measurements to prove its validity. Figures 35 and 36 give typical measurements showing the *reduction in the resting P_{O_2} -art due to lack of exercise*. For the strength and temporal effect of further stressful influences, the cases compiled in Fig. 37 should be consulted. It can be concluded from examples F and G from this figure that, in the combat of cancer by means of cancerostatics or radiation therapy, the application of O_2 MT is absolutely indicated as a protective measure to reverse the deterioration of the O_2 status, and thereby also to re-elevate the defence status. Examples in Fig. 38 show that the consequences of stressful

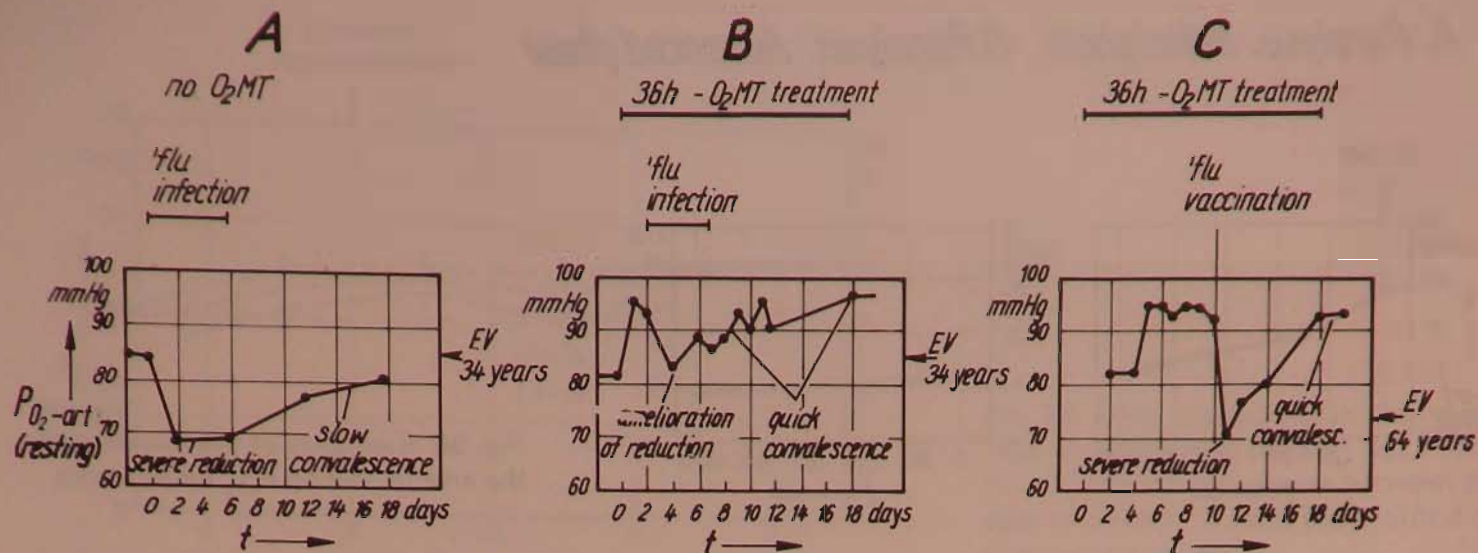


Fig. 38 Measurements of the change in arterial resting PO_2 (degeneration and regeneration of the lung heart-system) in a 'flu infection (A, B) and a 'flu vaccination without (A) and with (B, C) regeneration by means of O_2MT during infection phase. Examples. EV = expected value

influences can be ameliorated and combatted, if the O_2MT procedure is implemented *simultaneously*. It can be seen from the cases compiled that it is by no means only stressors such as those in Hans Selye's classical experiments, which cause depressions in the PO_{2-art} . Perhaps the concept of stress should be modified, following the findings discussed in this book.

Although one of the consequences of stress is a worsening, for a longer or shorter period of time, of the O_2 status (PO_{2-art} , PO_{2-ven} , η , O_2 uptake, CO_2 production, physical performance capacity, etc.), we have only discussed the in-

fluence of distress on the course of the PO_{2-art} here in great detail and supplemented with examples. The reason for this was, on the one hand, the convenient routine measurability of the course of the PO_{2-art} and, on the other, the fact that the inverse changes in the PO_{2-ven} are simultaneously triggered by the same capillary switching and regulating mechanism of the microcirculation. The changes in the PO_{2-ven} are thus mostly the approximate mirror image of the changes in the PO_{2-art} . The measurements of the course of the PO_{2-art} alone will only be insufficient when it is necessary to gain absolute

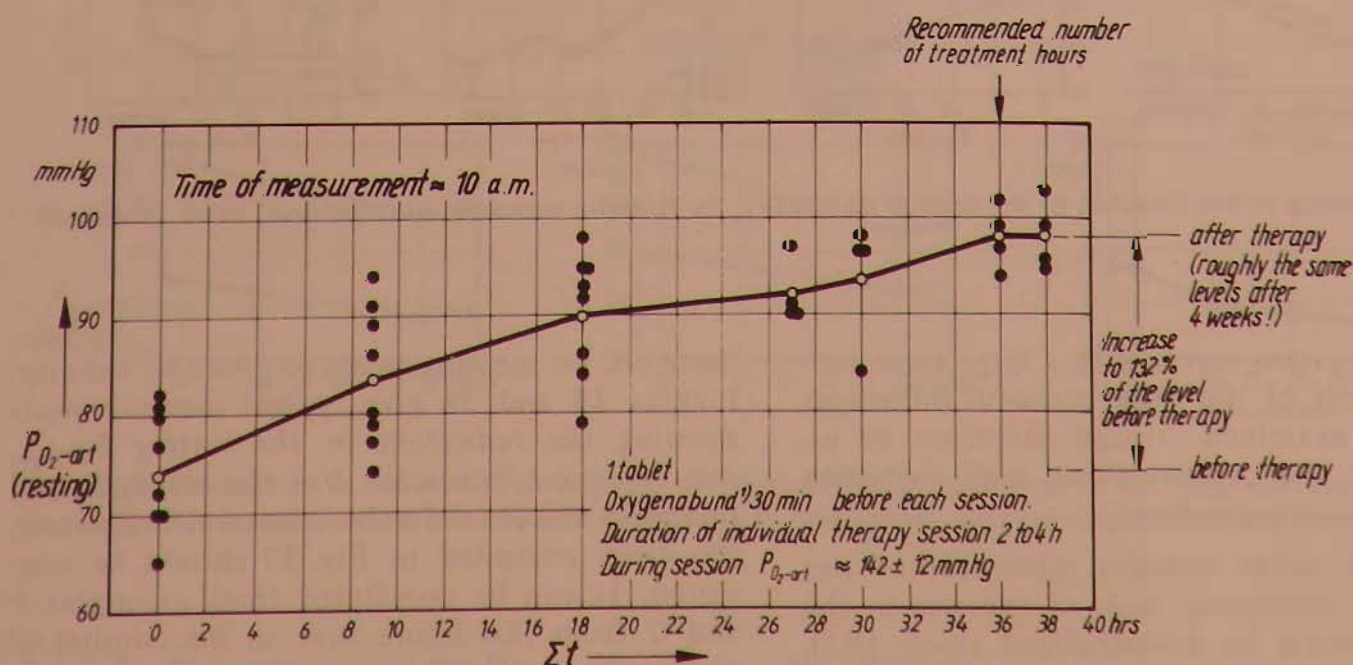


Fig. 39 Measurements of the arterial resting PO_2 as a function of the total no. of treatment hours ΣT of the O_2MT for healthy persons between the ages of 65 and 85 years. No. of persons $N = 8$. Mean values. Daily exercise training. Result: lasting increase of arterial resting PO_2 to 132% of the level before treatment

numerical values for the O_2 saturation difference η or for the O_2 status Q_{O_2} . In practice, matters are very much simplified by the fact that the simple measurement of the resting PO_{2-art} levels is usually enough to make pos-

sible assessment of the strength, temporal course and elimination of the consequences of distress, and to signal the necessity of O_2 MT repetitions.

1.1.8.4 The increase in the PO_{2-art} by means of O_2 multistep therapy procedures and exercise

In the implementation of O_2 MT procedure (variant GK 4-I) with exercise programmed for 2 min roughly every 20 min, and if possible with exercise training in the intervals between the sessions (step 1 and 2), there usually results an increase in the PO_{2-art} to an upper limit level within 30 to 36 treatment hours. For this reason this variant is termed the 36 h O_2 multi-

step therapy procedure in this book. Typical measurements for this on persons of an old age are summarized in Fig. 39. A comparison with groups of subjects of various ages shows that the improvement in PO_2 is particularly successful in old persons, for whom the attainment of a good O_2 status is of primary importance (Fig. 40).

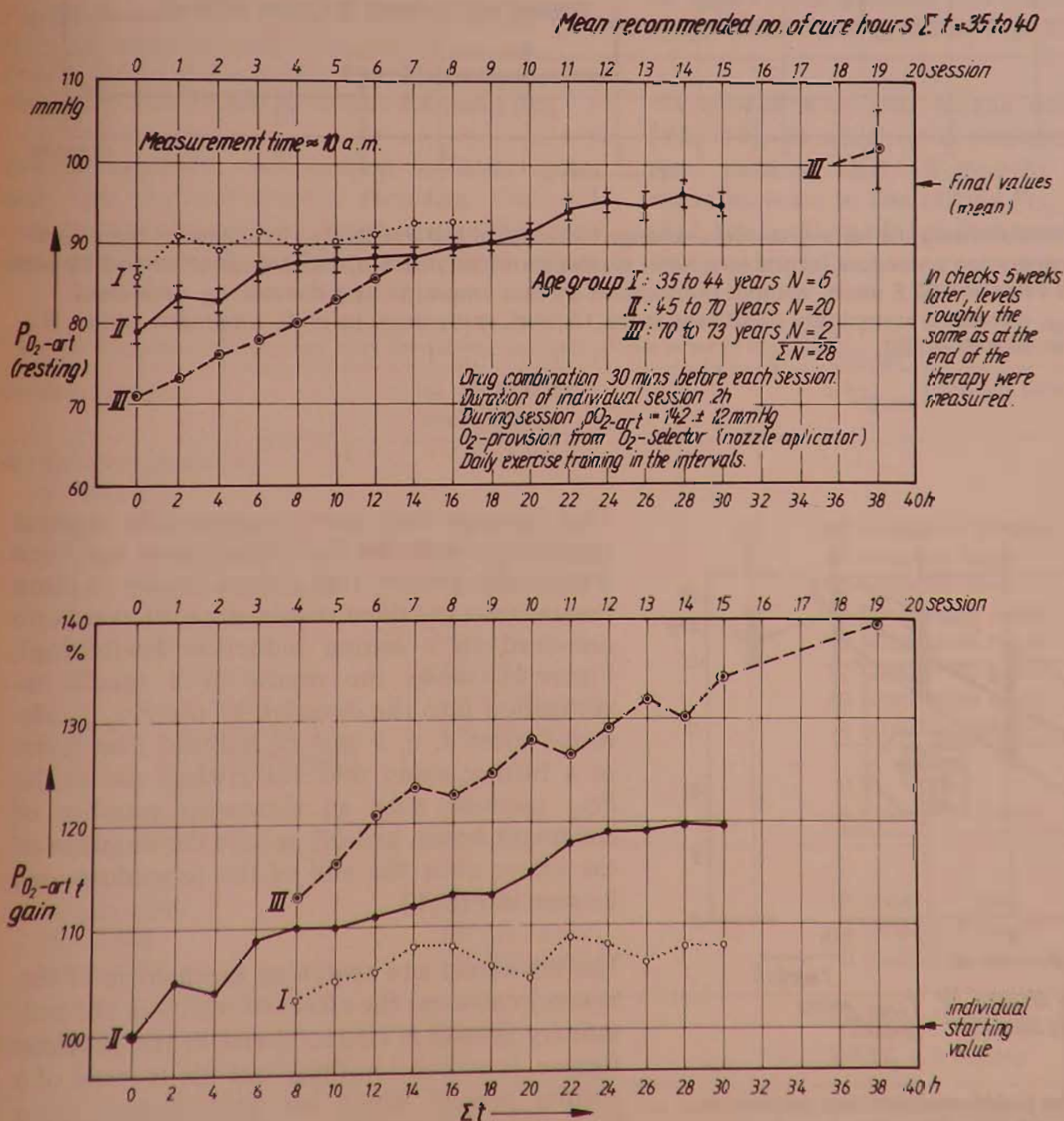


Fig. 40 Behavior of the arterial resting PO_2 as a function of the total no. of treatment hours Σt of O_2 MT in patients of various age-groups. No. of patients $N = 28$. Mean values $\pm$ standard deviation. Measurements H. G. Lippmann. Special series of experiments to establish the optimal no. of treatment hours. Measurements in sitting position (stan-

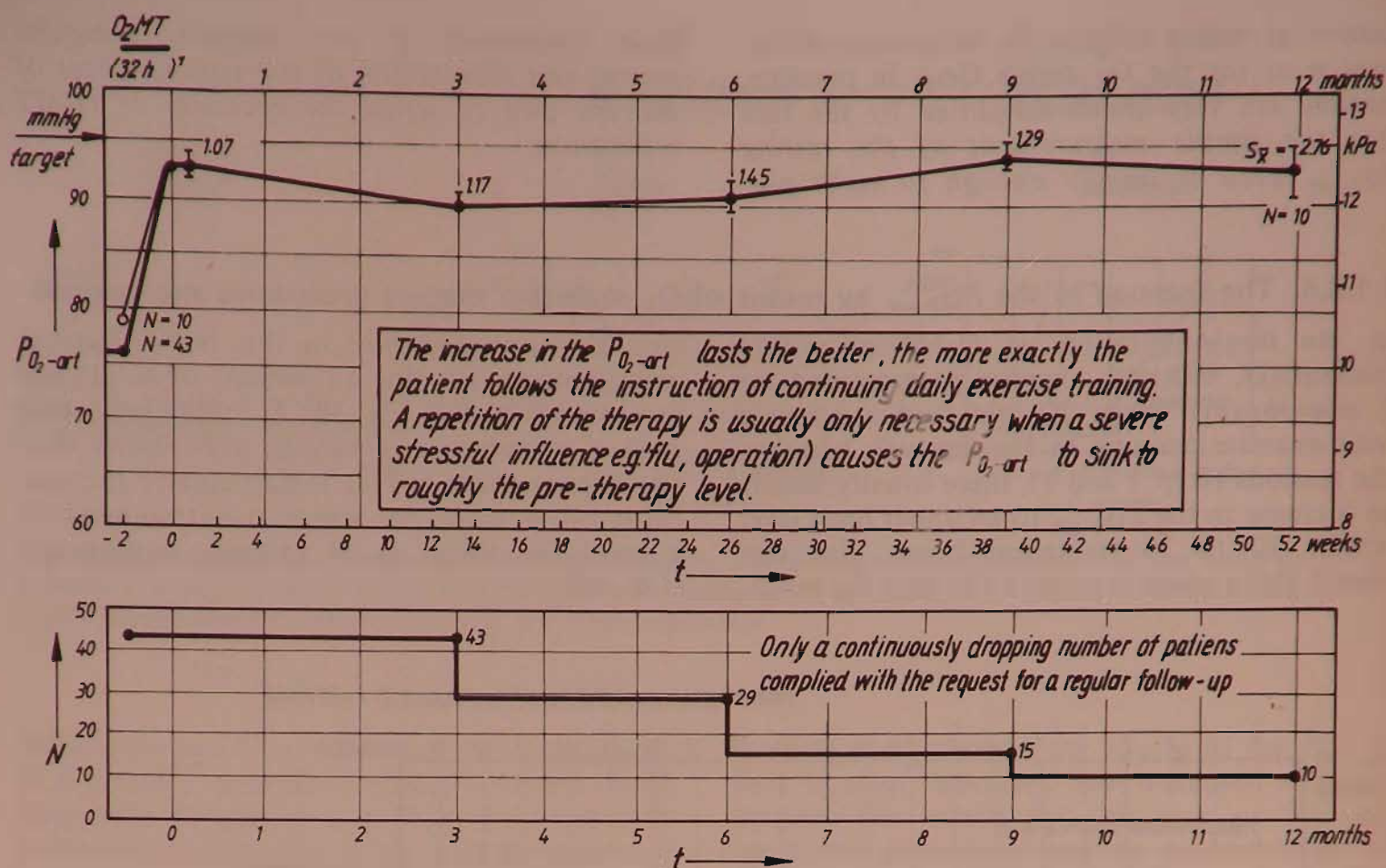


Fig. 41 Measurements showing the lasting, almost unchanged increase of the arterial P_{O_2} by means of the discovered functional regeneration procedure for the lung-heart system on initially 53 subjects (groups of 43 and 10 with a mean age of 65.3 years and 62.6 years) without pronounced chronic unspecific lung diseases. $s_{\bar{x}}$ = standard deviation; the O_2-art increase is statistically significant at the 1% level; study made by H. G. Lippmann and H. H. Wiemuth in our Institute 1979/80

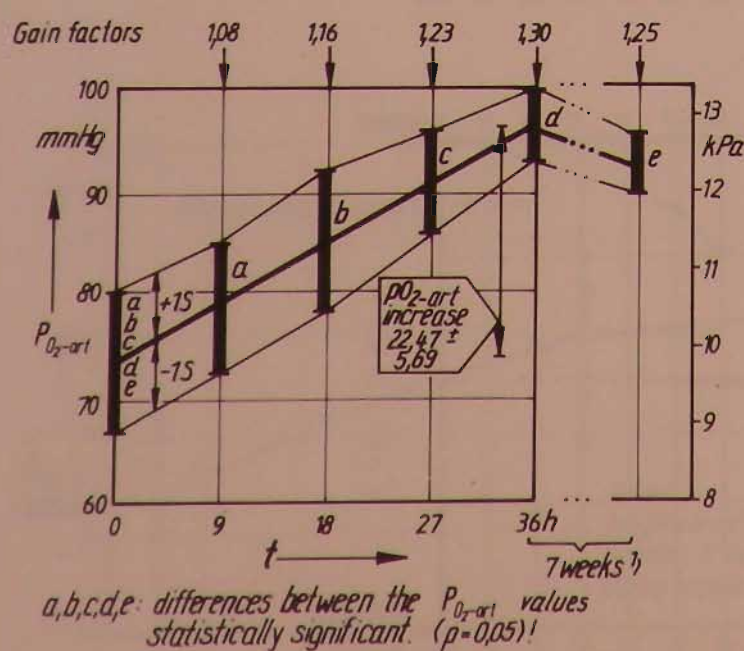


Fig. 42 Effect of the O_2MT regeneration procedure on the arterial resting P_{O_2} in 30 patients aged 65 ± 9 years with roughly normal blood pressure. Patients from non-specialized cure institutions

This increase only gains considerable medical significance with the fact, which now has been statistically proven, that it lasts for up to more than a year, provided severe stressful events do not lead to a lasting reduction (switching). Figure 41 shows the results of a special investigation into the duration of the P_{O_2-art} elevation after 3, 6, 9 and 12 months. The result of a further study into the gradual rise in the P_{O_2} increase with an increasing number of treatment hours, as well as into the duration of the effect after the end of the procedure, can be seen in Fig. 42.

The regulating and switching mechanism of the microcirculation, the effect of which in the pulmonary system is characterized in the previous figures, is actually nothing but the reversal of a natural process which has been known for a long time and has been largely explained by electron microscopy [89, 90]. We are referring to the process of the swelling of the endothelial cells in O_2 deficiency. Because this swelling is reversible, it declines with excess O_2 the

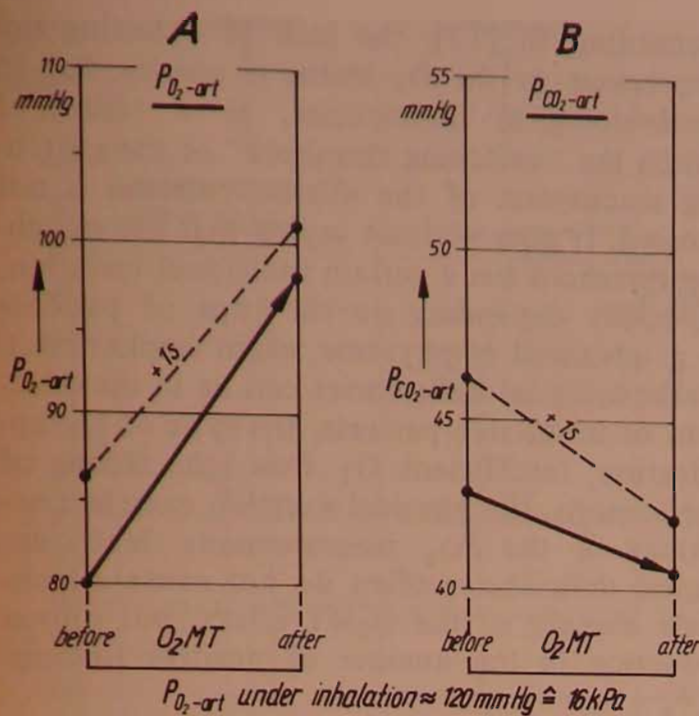


Fig. 43 Arterial resting levels of P_{O_2} (A) and the P_{CO_2} (B) before and after 30 hrs O₂MT cure procedure, represented as $\bar{x} + 1s$. N = 13. (Therapy responders with a mean age of 59 ± 9.4 years) [92]

rowest capillary cross-section extends again, and the microcirculation increases. Our discovery therefore refers to the *reversibility of this fundamental, natural mechanism which*

occurs in all capillaries of the human body, and also to the recognition and proof that the basis of this mechanism is formed by a feedback system with switching properties, which leads to the persistence of the bioenergetically triggered effect.

As has been mentioned above, the basic effect, the increase in the P_{O_2-art} or in the oxygen transport to the body tissue, has unfortunately been called into question by two studies made in foreign institutes with small numbers of patients, e.g. [91]. Since these negative findings met with an extraordinary response in various medical journals, centers in Dresden and elsewhere, which had been practising the O₂MT for some time, carried out studies with large numbers of patients into the question of the increase or non-increase in the P_{O_2-art} by means of O₂MT. The positive and evidential results of these studies are given in Fig. 43 and Table 4.

We should refer here to the works of Caspers [93, 94], in which it is established using 108 cure patients that 18 months after O₂MT a mean increase in the resting P_{O_2-art} of 6 mmHg (0.7 kPa) still exists, as compared with the pre-therapy level.

Table 4 Results of 12 studies into the lasting increase of the arterial P_{O_2} (ΔP_{O_2-art}), at rest, by means of O₂MT

studies, authors	no. of patients (mean age)	ΔP_{O_2-art} [mmHg] time
A 3rd German edition of this book		
p. 35 von Ardenne	8 (72 years)	22 (also after 30 days)
p. 37 Lippmann	43 (64 years)	14 (after 90 days)
p. 37 several sanatoria	30 (59 years)	13 (after 50 days)
p. 38 von Ardenne	13 (59 years)	18 (after some days)
p. 38 Wolf	108 (67 years)	19 (after some days)
p. 39 10 clinics	1407 (69 years)	12 (after > 30 days)
p. 44 von Ardenne	5 (~ 60 years)	16 (after some days)
p. 67 von Ardenne	15 (58 years)	4 (after > 1 day) ¹
p. 317 Schnizer (Fulgum)		
1981	38	0
1982 (!)	27	9,4 (after > 1 day)
B further studies		
Caspers 1985	938 (67 years)	13 (after > 1 day)
Wolf 1985	88 (62 years)	14 (after > 1 day) ¹
Nolte 1980	22 (62 years)	0 (failure to reach switching threshold)
comparison: 11 studies		$\Delta PaO_2 = 14$ mmHg (!) or 1,8 kPa
1 study (Nolte)	22	$\Delta PaO_2 = 0$ mmHg

¹ The average lowering of the P_{O_2-ven} (ΔP_{O_2-ven}), at rest, in these studies was -10,3 mmHg (v.A.) or -15 mmHg (W)

An assessment of the effectiveness of the O₂MT without including measurements of the changes occurring in the venous P_{O_2} is not possible! This basic principle was ignored by some authors (Nolte, Hendrik, Schnizer), resulting in false assessments of effectiveness.

gered, which considerably contributes to the fast, large increase in η , i.e. to a great increase in the O_2 transport to the body tissue.

In the investigation into the contribution of the individual steps to the entire effect, one of the questions which we examined was that of the increase in η due to physical exertion. As a control in the program of the O_2 MT quick procedure, O_2 application and drug administration were omitted in 3 further individuals. An increase in η , on average only slight and quickly declining, was then found (training effect). *The switching process of the microcirculation with its lasting effect was not triggered by 100 W physical exertion alone.* In contrast to the result in Fig. 44 right, an increase in the PO_{2-art}

after strenuous exercise training was generally also observed, if the strong physical exertion was repeated on several consecutive days. Figure 45 gives an example of this type. The threshold of the switching function can be crossed and a lasting PO_2 effect achieved, as documented by part "d" of the curve shown in Fig. 17, by means of strong exercise training (daily 3 h gardening) over 1–2 weeks, e.g. mowing the lawn.

In older age and in the case of disease, the capacity for high-charging of η by means of stamina training or intensive sport alone is drastically reduced. Variants of the O_2 MT, adapted to the individual performance capacity, are then to be chosen.

1.1.8.5 The level of PO_{2-art} and η , and its relation to the amount of circulatory reserves

In the discussion of our O_2 MT research the following view has been repeatedly expressed by thoroughly competent persons. It was said that the aimed for increase in the PO_{2-art} could bring about no improvement, as the gain in saturation attainable even in old age was only 4%, and the reduced PO_{2-art} in old age was still sufficient to saturate the arterial blood almost completely with oxygen. This view is wrong for several reasons:

1. The gain of 4% must be seen in relation to the fact that the arteriovenous exhaustion of the O_2 binding capacity of the blood is only 20%. Hence, an increase of an additional 4% in the O_2 transport means 1/5 more as compared to the original 20%, and that is a great deal in stages of weakness.
2. The O_2 supply to the arterial walls, necessary for the maintenance of a good arterial vessel system (good O_2 supply to the tissue), occurs mainly due to O_2 diffusion from the lumen of the arteries and is therefore determined directly by the PO_{2-art} .
3. The triggering of critical conditions, as was already pointed out above, does not generally occur when the arteriovenous saturation difference η on the HbO_2 dissociation curve corresponds to the expected value for that age under normal conditions, but when the value of η , particularly when near to the minimum in the circadian cycle, sinks far below the expected value, due to acute stressful events (e.g. infections, toxic stress, reduced cardiac performance, hypoxemia during sleep, high fever, chronic CO poisoning etc.). The more the mean level of the PO_{2-art} and η are raised, the greater the cir-

culatory reserves and the smaller the probability that O_2 deficiency crises (e.g. dizziness, Ménière's disease, collapse, attacks of angina pectoris, myocardial infarction) will be triggered.

Figure 46, especially, the patient examples on the left, gives a quantitative basis to the statement in the last paragraph. It is assumed in case B that the starting level of the resting PO_{2-art} is 72 mmHg (9.6 kPa), which roughly corresponds to the mean expected level for a 72-year-old. It follows from the further drawn scale of the HbO_2 saturation of the blood (standard conditions 37°C, pH 7.4) that the degree of saturation is then still $SO_2 = 93.3\%$. As the further scale of the utilization of the O_2 binding capacity of the blood shows, this corresponds to $\eta = 20.3\%$, taking as a basis the normally applicable mixed PO_{2-ven} of 40 mmHg (5.3 kPa). The numerical values named, characterizing a circulatory condition which is still just about good enough, are drastically reduced when, as a consequence of stressful influences, a temporary drop in the PO_{2-art} and a rise in the PO_{2-ven} are triggered. The case B in our figure shows just how severely the numerical value of η , the PO_{2-art} , and the O_2 saturation of the blood can deteriorate in such cases. The working points on the various scales shift to deep within the dangerous zone. The circulatory reserves converge towards zero.

A much more favourable situation exists in case A in Fig. 46. When the starting level of the resting PO_{2-art} is high (between 95 and 100 mmHg $\triangleq$ 12.7–13.3 kPa), the O_2 saturation is almost 97% and the exhaustion of the O_2 binding capacity of the blood approximately

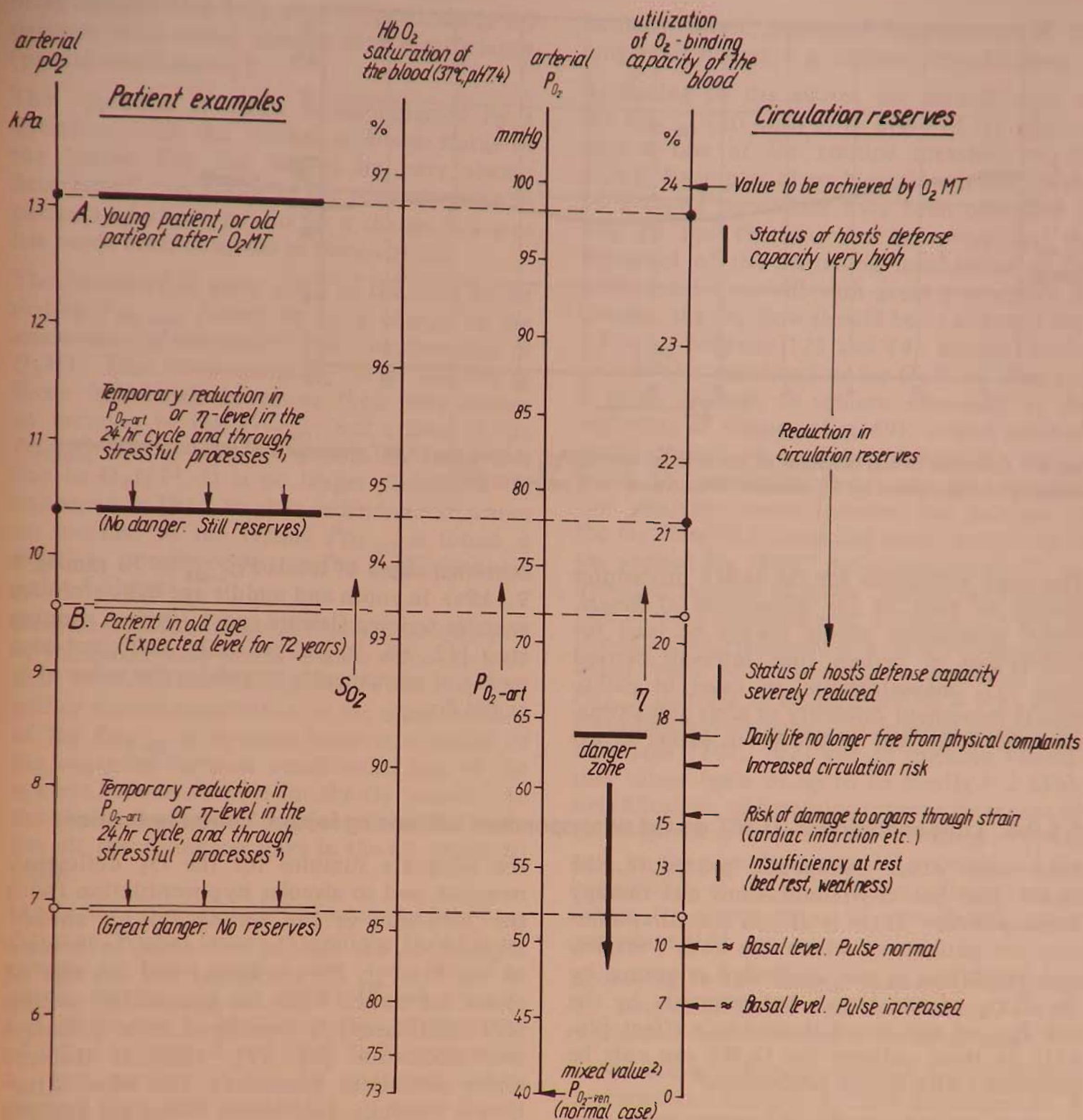


Fig. 46 Quantitative representation of the drastic reduction of the dangers of stressful events in older persons through permanent increase of the utilization coefficient η of the O_2 binding capacity of the blood. Guiding values²

¹ Assumption on the basis in our measurements of the reduction in P_{O_2-art} or η -level during stressful events of very different kinds.

² In subjects with a long-term very low P_{O_2-art} ($\approx < 70$ mmHg). Nature usually responds with improved O_2 utilization. Then the assumption of a mixed $P_{O_2-art} = 40$ mmHg is no longer valid and both scales on the left shift upwards, corresponding to the drop in the P_{O_2-ven} .

24%. Most importantly, however, in a temporary drop in the resting P_{O_2-art} or η , due to the stressful influences during the 24 h cycle, the working points do not shift as far as the danger zone. Considerable (circulatory) reserves exist in patient A, even in such a phase.

We have already been able to document cases

where in very old patients (similar to example B in Fig. 46), from P_{O_2} measurements, increased pulse, as well as the occurrence of immobility and dizziness, a potentially fatal condition was apparent. The immediately implemented O_2 MT procedures eliminated these symptoms and have since led to an extended lifespan of already several years.

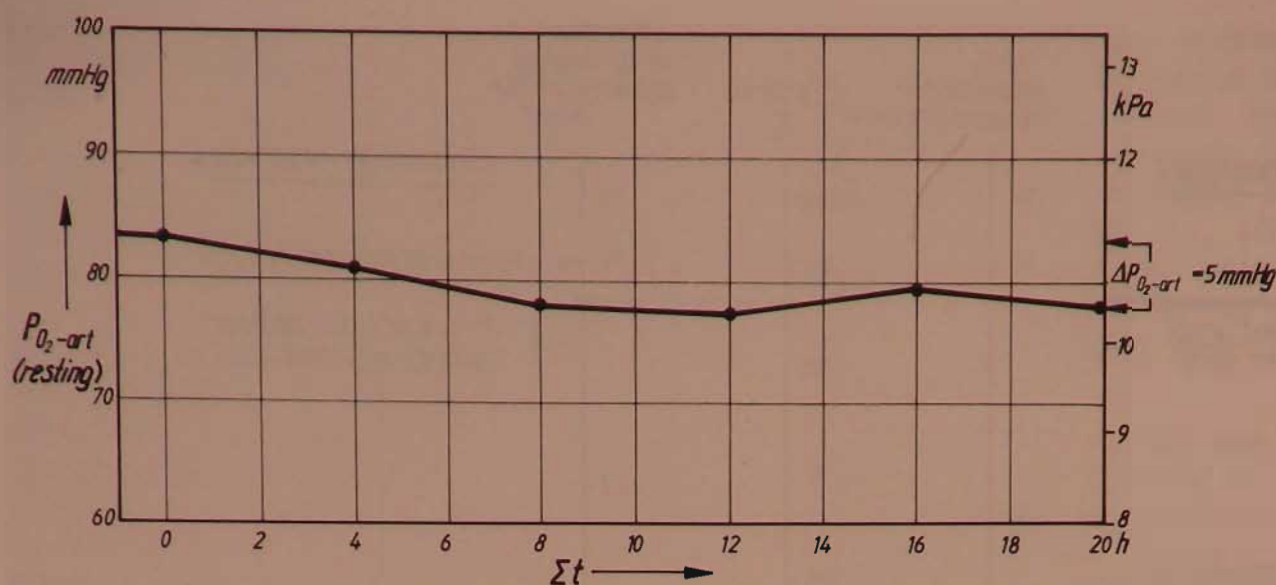


Fig. 47 Example of the behavior of the arterial resting PO_2 during the O_2MT treatment of real nonresponders (slowing of respiration by O_2 excess). Mean values of 3 patients [92]

The main indication for the O_2MT procedures should be seen as the *prevention of illness*. These procedures should always be used for prophylaxis at certain time intervals derived from PO_2 measurements, in cases of pathological movement disability or after approximately the 55th year of life (even earlier in ex-

ceptional cases of levels $PO_{2-art} < 70$ mmHg $\triangleq$ 9.3 kPa). In youth and middle age daily strenuous exercise training (leisure sport, jogging, running etc.) [12, 88, 95] is generally sufficient as a means of permanently increasing the value of η , or the PO_{2-art} .

1.1.8.6 Lung-conditioned, O_2MT partial nonresponders; influencing factors, contra-indications

Like every other therapeutic procedure, the O_2MT also has contraindications and therapy nonresponders. There is usually a *contra-indication* for patients in whom the body's respiratory regulation is not controlled as normal by the PCO_2 of the blood, but primarily by the low PO_2 of the blood (Loeschke's effect [96, 97]). In these patients the O_2MT can only be performed with special precautions¹.

In some patients, as Fig. 47 shows, even a reduction in the arterial resting PO_2 of roughly 5 mmHg due to the O_2MT procedure was observed. In these patients a drop in the PO_{2-ven} under O_2MT must have been attained.

As is known [96, 97], the arterial hypoxemia which exists in generalized respiratory insufficiency is associated with an O_2 deficient control of ventilation. Application of O_2 eliminates

the adequate stimulus for the O_2 deficiency receptor, and so alveolar hypoventilation (with the reduction in the resting PO_{2-art} already mentioned), and also, in such cases, an increase in the PCO_{2-art} (hypercapnia) and the risk of apnea can occur. When the generalized respiratory insufficiency is considered to be a relative contra-indication [98, 99], which is absolute under outpatient conditions, and when attention is carefully paid to the blood gas analysis and the acid-base balance in partial respiratory insufficiency, where we have never observed any dysfunctions, the O_2MT has proven its principal applicability under these circumstances, too. The temporary inhalation of oxygen in patients with chronic lung diseases and consecutive cor pulmonale has been successfully practised with the aim of reducing the resistance in the lesser circulation for years [100]. Whether, and to what extent, the O_2MT could have a comparable effect, is to be the subject of future investigations, appropriately in pulmologically oriented treatment centers. However, there can hardly be any risk for the patient in our therapy program with only a doubling or trebling of the O_2 content in the inhalation air in the 36 h procedure. The O_2MT , or the technology developed for it, can

¹ Artificial respiration if necessary. Recognition of patients with abnormal respiration regulation by means of initial test, e.g. with checking of the blood gases. For the dangers of artificial respiration for patients with severe chronic respiratory insufficiency using O_2 air mixtures with O_2 proportions $> 50\%$ (respiratory depression, arterial PCO_2 60 mmHg, respiratory acidosis), see [98, 99].

offer considerable help even to (particularly to) patients with severe chronic lung insufficiency (partial insufficiency).

The approach of crises is accompanied by a deviation from the normal acid-base status of the blood. For this reason we have always determined this status in the research phase in patients of this type. So far a change in status has never been observed in these checks.

The discovery in early 1982 of the drop in the resting PO_{2-ven} forced us to a *change in the assessment of responders and nonresponders to O_2 MT*. True nonresponders can be defined as those individuals in whom there was neither an increase in the PO_{2-art} , nor a drop in the PO_{2-ven} , i.e. no improvement in the value of η due to O_2 MT¹. It is no longer permissible, as happened in [91], to class individuals in whom no increase in the resting PO_{2-art} is found, a priori as nonresponders to the O_2 MT (see also Table 5 above).

Despite this fundamental finding, the question of the *influencing factors on the responder rate with reference to the increase in the PO_{2-art} is still of topical significance*, as the absolute value of the PO_{2-art} is in some important tissues of the organism (arterial vessel walls, lens of the eye etc.) alone decisive for the O_2 transport to the tissue, and good lung function alone benefits all the following links in the O_2 transport chain.

Indications of factors influencing the lung-conditioned, partial failure rate of the O_2 MT were already be taken from a pilot study [92]. The study, carried out on 46 unselected patients (29 males and 17 females) within an age range of 34–75 years ($\bar{x} = 55.9 \pm 11.3$ years), with a total number of 20–30 treatment hours, showed that, with a mean PO_{2-art} under O_2 inhalation of 115.3 mmHg ($\hat{=}$ 15.36 kPa) instead of 125 mmHg ($\hat{=}$ 16.7 kPa), the failure rate rose from between 15 and 20% to 33%. It is certainly no coincidence that in the group with a high proportion of non-responders (failure rate 60%), a mean PO_{2-art} of 105.5 mmHg ($\hat{=}$ 14.1 kPa) was established during inhalation. It can be seen from these findings that the success rate in the application of the 36 h O_2 MT procedure drops quickly when PO_{2-art} under inhalation remains below 125 mmHg ($\hat{=}$ 16.7 kPa) (oxygen flow too sparingly applied, e.g. < 3 l/min; par-

ticularly severe, advanced degeneration of the lung-heart system, e.g. chronic bronchitis).

According to the above, the measurement of the PO_{2-art} (20 min) after begin of O_2 application is one of the routine measures of the O_2 MT. Examples of such measurements for the 36 h O_2 MT procedure have been compiled in Figs 48 and 49. In order to ensure that the threshold of the switching mechanism of the microcirculation will with great probability be crossed, the O_2 flow should be so adjusted that a PO_{2-art} between 125 and 145 mmHg (16.7–19.3 kPa) is measured under O_2 flow. This aim is often difficult to achieve, especially at the beginning of therapy (Fig. 49). In such cases *all means should be used to increase the PO_{2-art} under O_2 inhalation during the first sessions*. The adjuvant means include: the increase of the O_2 flow to 5 l/min and more; activation of the applied O_2 , HOT* procedure during O_2 inhalation; increase in blood fluidity; administration of 0.5 g nicotinic acid; drinking of a cup of strong coffee; treatment in a lying position with upper body at a lower level (resulting in a PO_{2-art} increase of up to 6 mmHg $\hat{=}$ 1.33 kPa); preceding physiotherapy to improve respiratory technique [101, 102] and to improve ventilation values (gain of up to 15 mmHg $\hat{=}$ 2 kPa); simplification of breathing training by means of the respiration biofeedback instrument [103] and, in chain smokers with CO poisoning of the hemoglobin of up to 20%, preceding detoxification by means of a 15 min O_2 MT quick procedure [18].

According to the findings discussed, the group of *lung-conditioned partial therapy non-responders* can be divided in six subgroups:

1. Structural pulmonary diseases with diffusion disorders, namely, in the existence of a generalized respiratory insufficiency. The proportion of such cases in nonselected patients is less than 10%.
2. Cerebrovascularly decompensated patients lacking compliance due to an organocerebral psychosyndrome.
3. Patients with a high proportion of shunt volume in the lung.
4. Individuals with severe CO poisoning (e.g. chain smokers).
5. Cardiopulmonally decompensated patients: a recompensation is a prerequisite here for the implementation of the procedure.
6. In persons with a high PO_{2-art} over 90 mmHg $\hat{=}$ 12 kPa, e.g. due to physical stamina training), a higher level cannot be expected to be achieved.

¹ There is even a certain therapy success when the PO_2 levels remain the same, if a reduction in the cardiac output can be recognized (less strain on the heart).

O_2 -flow to be set for $P_{O_2\text{-art}} > 125$ < 125 mmHg

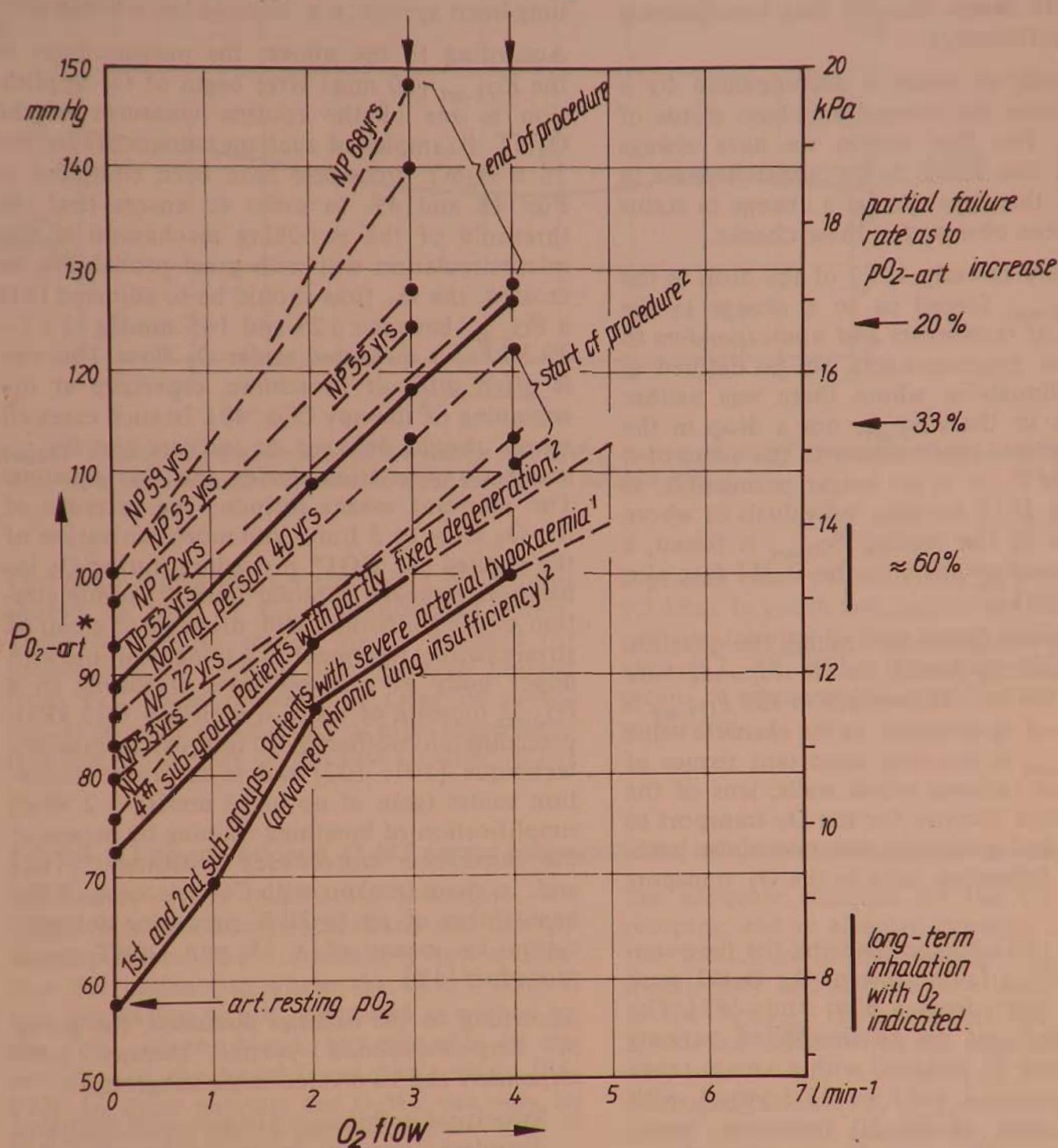


Fig. 48 The level of the resting P_{O_2} resulting 20 min after start of O_2 inhalation via the O_2 wasting (outdated) nasal cannula as a function of the O_2 flow for various types of patients (measurements taken in a sitting position). The $P_{O_2\text{-art}}$ value to be attained during the individual sessions of the 36 h O_2 MT should be > 125 mmHg

¹ To be supplemented by respiratory therapy [102, 103]; check $P_{O_2\text{-art}}$ (< 40 mmHg)

² Patients of these groups should breathe oxygen at the beginning of the first sessions in a lying position with the head directed downward, in order thereby to raise the $P_{O_2\text{-art}}$ level under O_2 inhalation by about 6%

The factors influencing the rate of lung-conditioned partial therapy nonresponders for the 36 h O_2 MT procedure was quantitatively investigated in a special study [104]: after multiple control measurements on the same person on the same and consecutive days always at the same time of day, the P_{O_2} levels measured in blood samples were around 80 mmHg (10.7

kPa), and mean deviations were below 3 mmHg (0.44 kPa). With the inclusion of a short safety span we can thus speak of an increase in the $P_{O_2\text{-art}}$, when an increase of more than 5 mmHg (0.67 kPa) is measured in repeated controls. Proceeding from this, we would like to give the following definition:

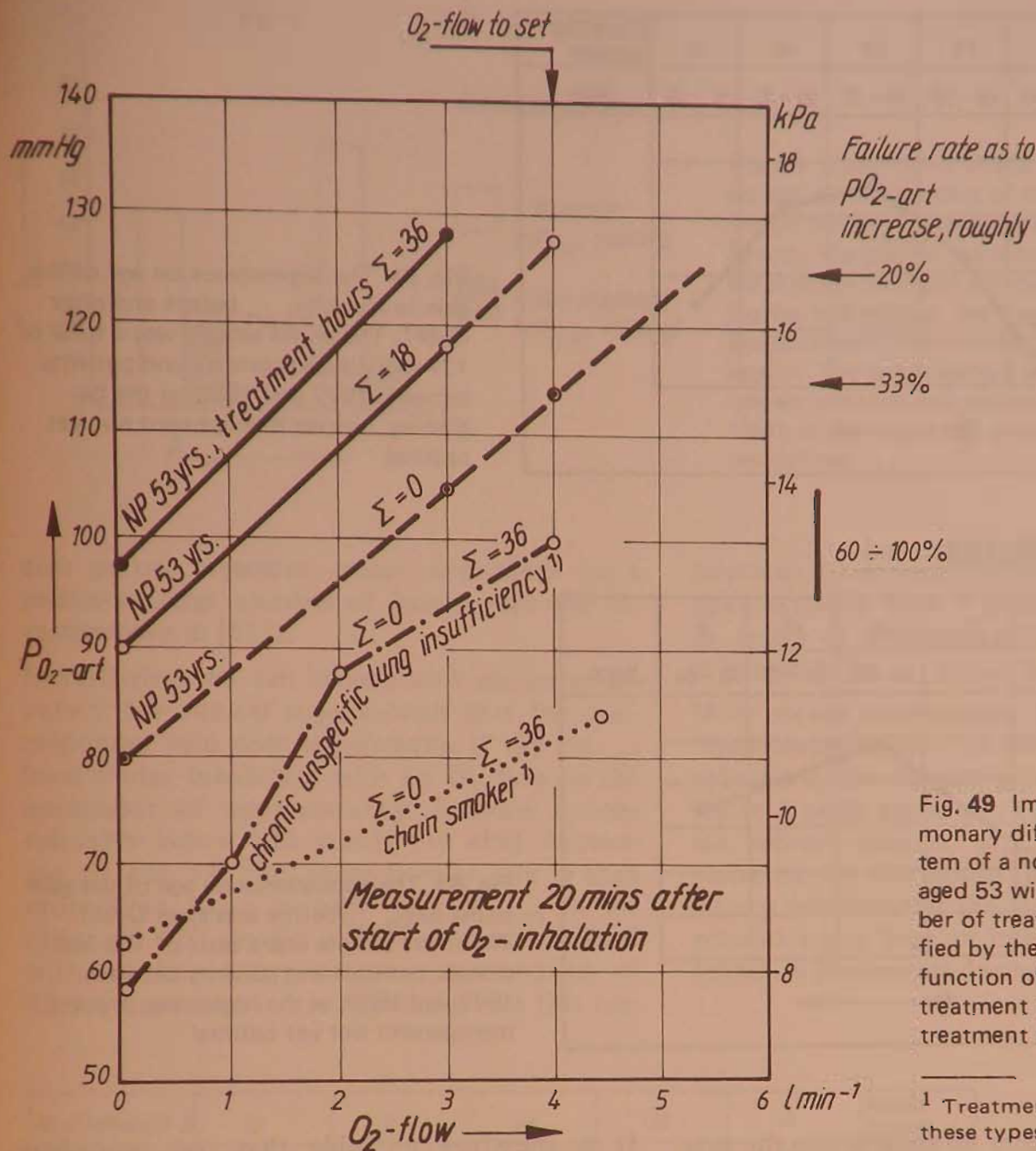


Fig. 49 Improvement of the pulmonary diffusion/perfusion system of a normal person (NP) aged 53 with the increasing number of treatment hours, exemplified by the P_{O_2-art} at rest, as function of the O_2 flow during treatment in dependence on the treatment time

¹ Treatment not indicated for these types of patients

A P_{O_2-art} responder is an individual in whom, after O_2 MT, the P_{O_2-art} under resting conditions is measured at more than 5 mmHg (0.67 kPa) higher than before O_2 MT. A therapy nonresponder is a person in whom this increase is not achieved. The non-

responder rate is the proportion (in per cent) of patients without response among the total number of individuals in the group under consideration. Correspondingly, the responder rate is the proportion (in per cent) of responders in the population under consideration.

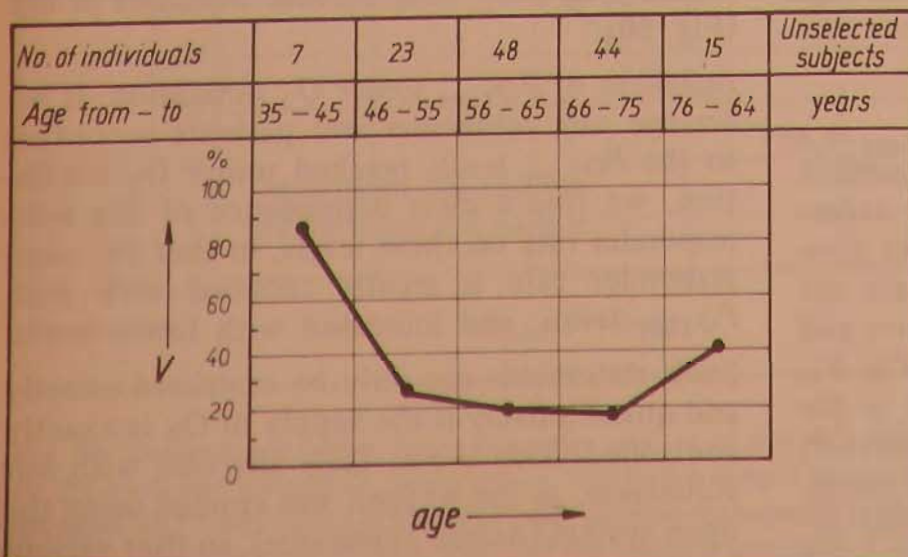


Fig. 50 Dependence of the non-responder rate (V) of the 36 h O_2 MT process on age (discriminative index: $\Delta P_{O_2-art} < 5$ mmHg). 137 individuals tested between 1977-80; treatment conditions partially not yet optimal at the beginning of the series

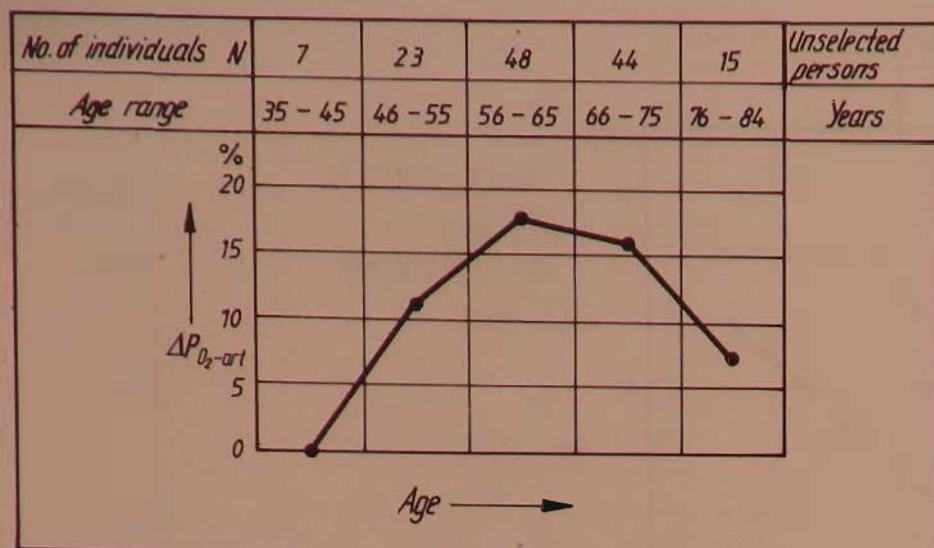


Fig. 51 The dependence on age of the gain in the ΔP_{O_2-art} before and after O_2 MT. The entire sample was a total of 137 individuals; controls and patients between 1977 and 1980; at the beginning, process management not yet optimal

Responders only

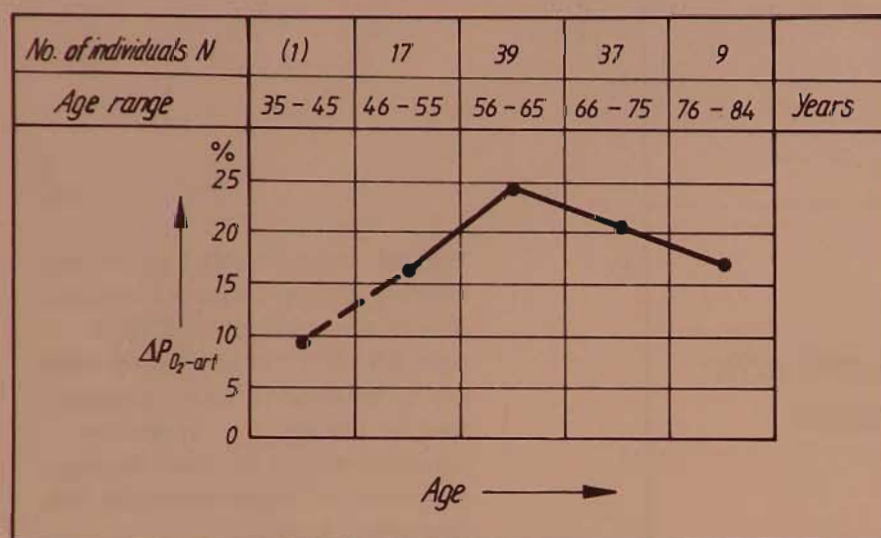


Fig. 52 The dependence on age of the gain in the ΔP_{O_2-art} before and after O_2 MT. The entire sample was a total of 103 individuals; controls and patients between 1977 and 1980; at the beginning, process management not yet optimal

Influence of age. Figure 50 summarizes the percentage of nonresponders V for all treated persons, dependent on age. A dependency on age can be clearly seen, inasmuch as a lower age limit can be defined, below which therapeutic success, in the sense of a rise in P_{O_2-art} , can only be expected in exceptional cases. It can further be seen that a positive response with a low nonresponder rate is possible in the age range from 46 to 75 years. Above this age group we must again reckon with a higher nonresponder rate.

Figure 51 shows the relative gain in P_{O_2-art} as a per cent of the starting level for all examined persons. The drop in the gain in the oldest group is primarily a result of the higher nonresponder rate. If we therefore eliminate the non-responders from the same population and present the gain in the same way as in Fig. 52, then the gain should correspond to that of the younger group. That is not the case, however, as the figure shows. The gain already drops from the age groups of 66- to 75-year-old individuals.

It is therefore probable that our procedure encounters limits here which are primarily pulmonarily conditioned. The regeneration procedure no longer succeeds with full intensity in cases of manifest, morphologically fixed disorders. This is expressed in increasing age at first only in a reduction in the attainable gain (Fig. 52, start of reduction already in the 66- to 75-year group), whilst the nonresponder rate rises significantly with further increases in age (Fig. 50).

Influence of P_{O_2-art} under O_2 inhalation. If we arrange our volunteers and patients according to the P_{O_2-art} levels reached under O_2 inhalation, we find a clear dependence of the nonresponder rate on these levels, in that the nonresponder rate is greatly reduced with high P_{O_2-art} levels, and increased with lower levels.

Such statements can only be evaluated exactly and quantitatively if the supply of O_2 is exactly controlled. This is not fully the case with our volunteers, as the oxygen was applied using the open system (nozzle applicator), so that various

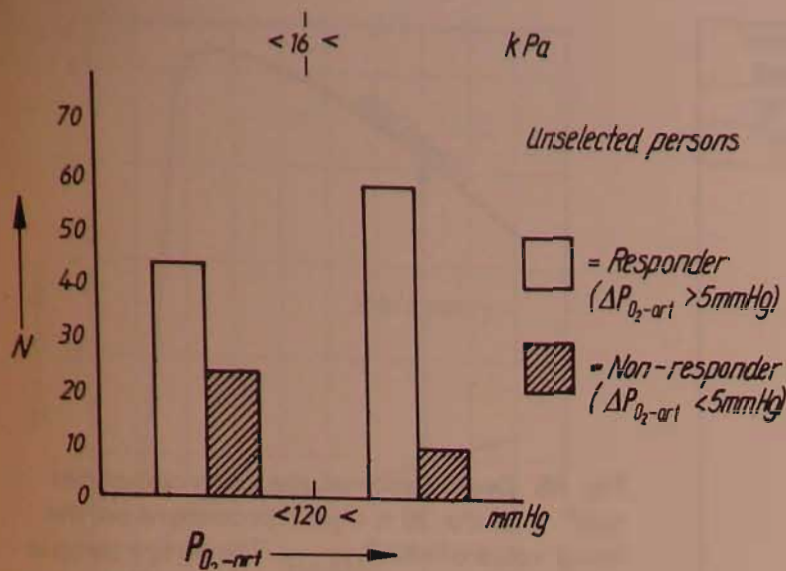


Fig. 53 Dependence of the number N of responders and non-responders of the 36 h O_2 MT procedure on the P_{O_2-art} measured during O_2 application. Result: The greater the increase in P_{O_2-art} between the starting level and the measurement level during the first session, the lower the failure rate. Measurement 20 min after the start of the first session. The entire sample was a total of 137 individuals; controls and patients between 1977 and 1980; at the beginning, process management not yet optimal!

also partial pressures, occur, dependent on a relatively large number of factors (see our investigations in [51]).

Nevertheless we can deduce with sufficient accuracy for clinical requirements that the non-responder rate rises significantly if the P_{O_2-art} level under inhalation with an O_2 flow to the applicator of approximately 3 l/min is considerably below 120 mmHg (16 kPa). According to Fig. 53, the nonresponder rate is then more than twice as high. If a P_{O_2-art} in the order of 120 mmHg cannot even be achieved with an inspiratory oxygen concentration of 40% (according to our measurements this cor-

responds to a mean flow of 5.6 l/min in the open system), then a positive effect of O_2 MT, in terms of a permanently increased P_{O_2-art} , is less probable.

More recent observations have shown that the "nonresponder rate" in terms of P_{O_2-art} can be reduced by the transition from a nozzle applicator to a mask applicator (with storage balloon, see below), because with this the O_2 is also delivered via the mouth (no uncontrolled temporary reduction of the O_2 flow when the test persons are talking, or in breathing through the mouth in treatments during sleep).

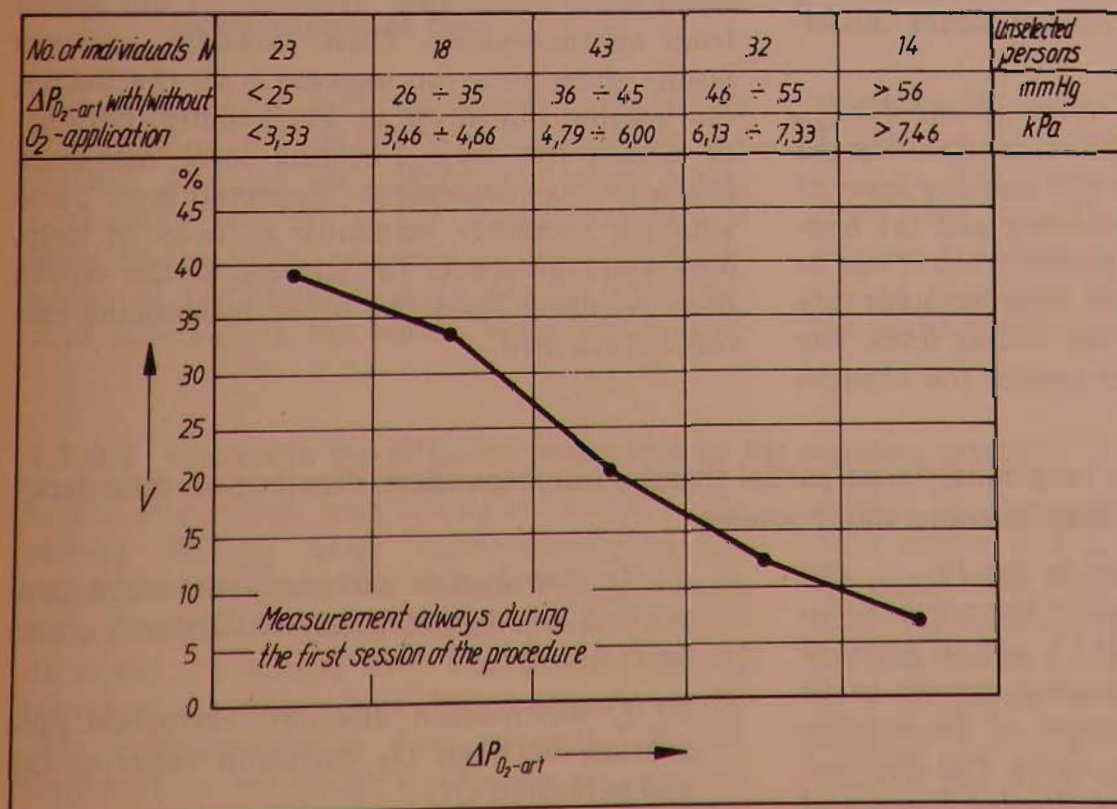


Fig. 54 Dependence of the "non-responder rate" V of the 36 h O_2 MT procedure on the increase in P_{O_2-art} (≈ 20 min after starting O_2 application). The entire sample was a total of 137 individuals; controls and patients between 1977 and 1980; at the beginning, process management not yet optimal. Result: The greater the increase between the starting level and the measurement level during the first session, the lower the failure rate

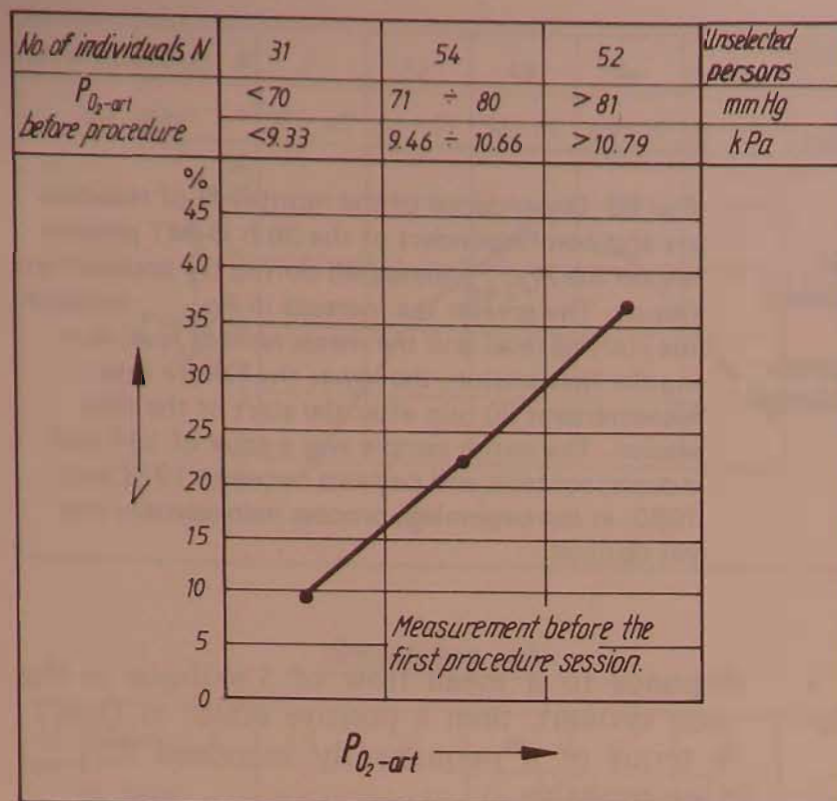


Fig. 55 Dependence of the "non-responder rate" V of the 36 h O_2 MT procedure on the initial value of the P_{O_2-art} . The entire sample was a total of 137 individuals; controls and patients between 1977 and 1980; at the beginning, process management not yet optimal. Result: The greater the increase in P_{O_2-art} between the starting level and the measurement level during the first session, the lower the failure rate

Influence of the initial increase in the P_{O_2-art} under O_2 inhalation. Closely connected to this is the rise in the P_{O_2-art} under the conditions named, in relation to the initial resting value. The greater this rise, the lower the non-responder rate, as in Fig. 54. It follows from this that patients with, for example, a low resting level and a relatively high increase under inhalation, can still be treated with a chance of success if the target level of 120–125 mmHg (16.0–16.7 kPa) is not reached under inhalation.

Influence of the starting level of the P_{O_2-art} before the procedure. If the values we obtained are arranged according to the starting level of the P_{O_2-art} before the procedure and the non-responder rate considered to this, then it can be seen, as in Fig. 55, that the nonresponder rate correlated positively with the resting level. The lower the initial value, the greater the chances

of success. This is the statistical evidence that youthful P_{O_2-art} levels are no indication for treatment.

The procedure's slim chances in individuals with an initially high resting value are easy to understand. It is not possible for the O_2 MT to increase the P_{O_2-art} levels to considerably above those which exist in youthful persons with healthy lungs. An increase can be attained when these levels have dropped, in old age or from another cause. Then, however, and our results show this, the increase is all the better, the greater this drop is. Particularly, patients in whom the P_{O_2-art} resting level has sunk below the age-dependent "expected level", and who are therefore primarily in need of help, have good prospects for success, if the conditions resulting from the other influencing factors are fulfilled.

1.1.8.7 Further causes for lung-conditioned partial therapy nonresponders; distribution disorders; proportion of the arteriovenous shunt volume

The causes of the reduction in the P_{O_2-art} and the corresponding increases in the mean diffusion-effective alveoloarterial O_2 partial pressure difference ΔP_{O_2} with increasing age are to be found less in the *deterioration of the ventilation parameters with age*, as in Fig. 56, and more in the *increase in the following functional disorders* [32, 80]:

1. *Diffusion disorder*: disturbed proportion between O_2 diffusion capacity D_L and perfusion (pulmonary blood flow) $\dot{Q}$.

2. *$\dot{V}_A/\dot{Q}$ distribution disorder*: disturbed proportion between alveolar ventilation $\dot{V}_A$ and perfusion $\dot{Q}$.

3. *$D_L/\dot{Q}$ distribution disorder*: disturbed proportion between O_2 diffusion capacity D_L and perfusion $\dot{Q}$.

4. Increased arteriovenous shunt volume.

The perfusion $\dot{Q}$ of the lung capillaries plays an important role in these functional disorders. It is therefore understandable that the bioener-

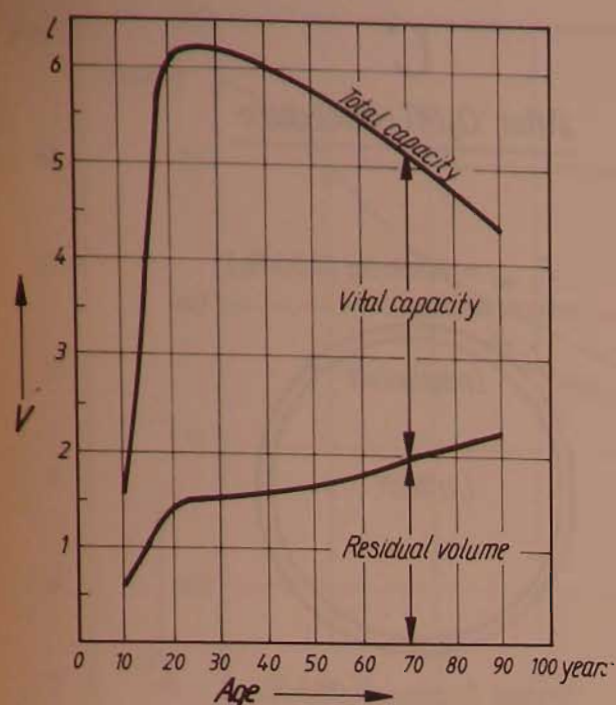


Fig. 56 Total capacity, vital capacity and residual volume of the lung, dependent on age in individuals of average size according to [32]

getically controlled regulating and switching mechanism of the blood microcirculation, discussed above, must have a great influence on the level of the $PO_{2\text{-art}}$, either positively (distension of the capillaries; O_2 MT, exercise training) or negatively (narrowing of the capillaries; persistent stressful influences). The high $PO_{2\text{-art}}$ reactivity of the lung is virtually lost in the partial nonresponders. According to the above explanations the reason for this can be a *para-*

lysis of the cellular vessel wall switching mechanism of the microcirculation, or a critical increase in the arteriovenous proportion of shunt blood in the lung. The first experimental findings on this very important problem for the maintenance of health resulted from a (non-voluntary) self-experiment [105, 106]. A nomogram for the determination of the arteriovenous shunt volume in the lung can be found in [107].

1.1.9 The effect of the cellular switching mechanism of the microcirculation in the other body tissue; effects of $PO_{2\text{-ven}}$

The finding that, with the change in the resting $PO_{2\text{-art}}$ due to O_2 MT, a counterchange in the resting $PO_{2\text{-ven}}$ simultaneously takes place, necessarily led us to the recognition that it must be the same regulating or switching mechanism of the blood microcirculation which occurs generally in the whole body, which is re-

sponsible for both changes. Such a mechanism, working in the whole body, has been unknown till now. The fluctuations in the resting $PO_{2\text{-ven}}$ show that the O_2 utilization in the tissue changes depending on the bioenergetically controlled thickness of the endothelial walls and hence the blood flow in the capillaries.

1.1.9.1 Change in the diffusion parameters of the capillary system

In the discovered, long lasting reduction of the resting $PO_{2\text{-ven}}$ after improvement of the energetic situation, the resting $PO_{2\text{-ven}}$ drops from, e.g. 40 mmHg (5.3 kPa) before, to levels of about 25 mmHg (3.3 kPa) after. The O_2 transport to the whole body tissue thereby rises considerably as does naturally the O_2 transport to the Krogh's cylinders surrounding the capillaries. How can this increase in O_2 diffusion be explained, despite the fact that, due to the reduction of the resting $PO_{2\text{-ven}}$, the difference in pressure decisive for the O_2 diffusion is considerably reduced? The qualitative

answer to this question is coarsely, schematically drawn in Fig. 57, for the venous end of the capillaries. When, before the O_2 MT procedure, the endothelial swelling has occurred and has led, due to a narrowing of the cross-section, to a reduction in the circulatory volume, the result will be a poor O_2 supply to the tissue, because the difference in O_2 pressure and the diffusion area, the latter of which is determined by the lumen, is reduced and, finally, the O_2 consumption in the thickened endothelium is increased.

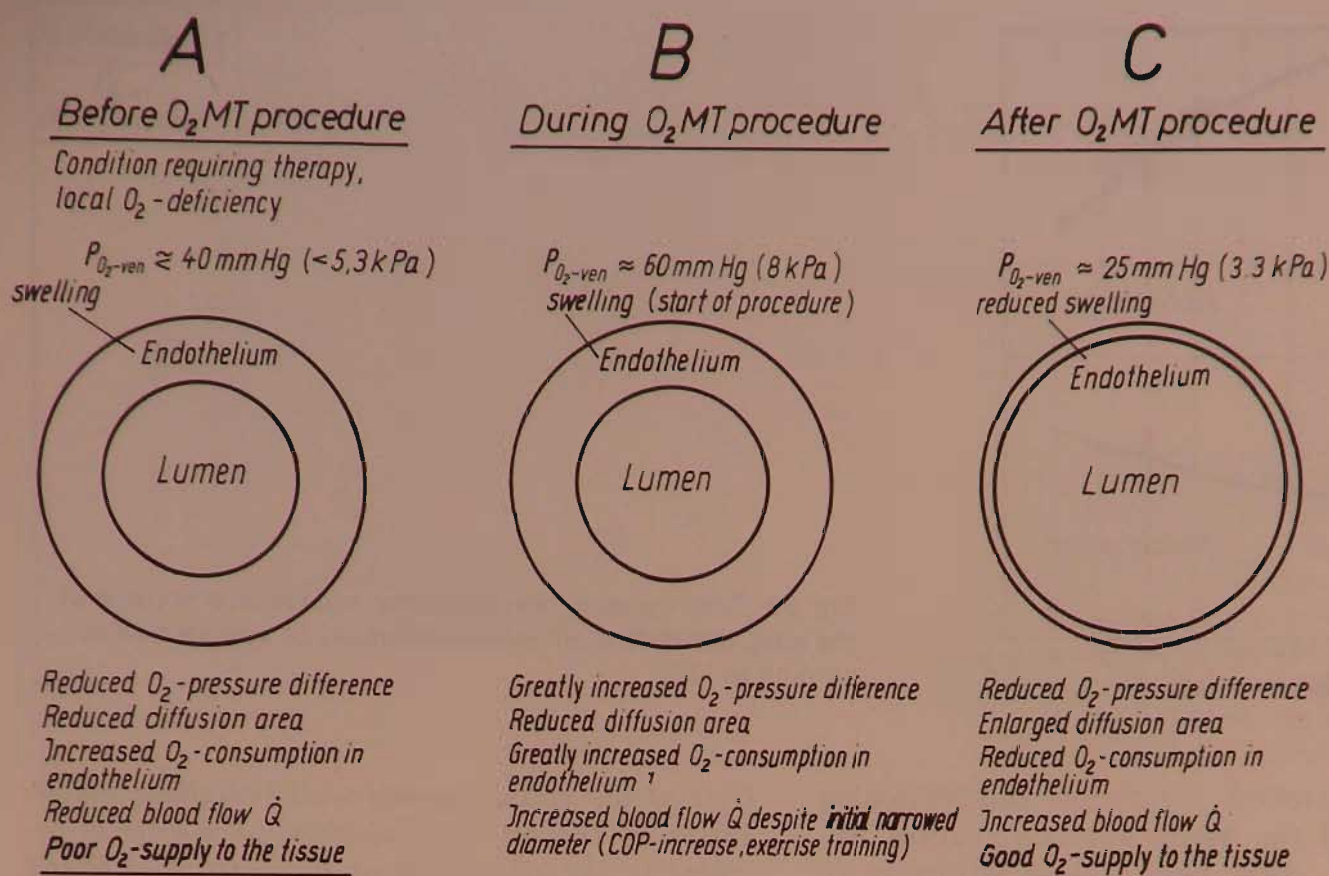


Fig. 57 O₂ diffusion parameters at the venous end of the capillaries before (A), during (B) and after (C) O₂MT. Rough schematic presentation. Example: 15 min O₂MT quick procedure

¹ Predominantly therapeutically effective for reducing endothelial swelling

The O₂ pressure difference is greatly increased during the O₂MT procedure, just as the volume of circulation is greatly increased by (simultaneous) physical exertion, with the result that an endothelial detumescence is triggered. When the endothelium has again reached its original size after the procedure, the diffusion area dependent on the lumen is simultaneously greatly

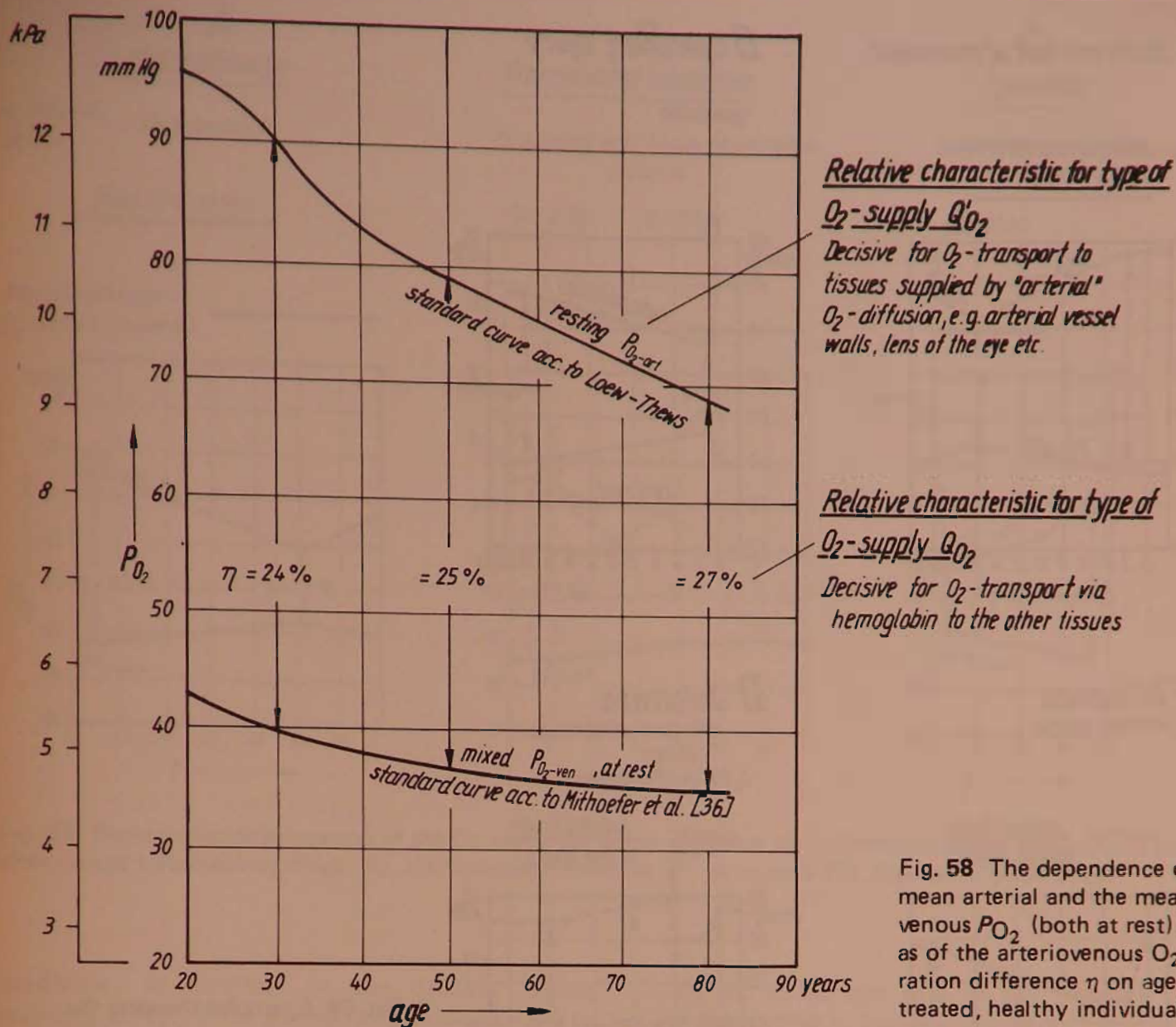
enlarged, the O₂ consumption in it reduced and the circulating volume has greatly increased due to the enlargement in the cross-section. The positive changes evidently overcompensate for the influence of the reduction in the O₂ pressure difference, so finally an improvement in the O₂ supply of the tissue surrounding the capillaries results (see also Fig. 6).

1.1.9.2 Slight drop in the $PO_{2\text{-ven}}$ with age; dependence of the η -value on age

From the overview of a very large number of resting $PO_{2\text{-ven}}$ measurements in volunteers of all age groups it could be seen that, in persons with a particularly low resting $PO_{2\text{-art}}$ the resting $PO_{2\text{-ven}}$ was, as a rule, also somewhat reduced. The organism evidently responds to a reduction of the O₂ saturation of the blood with an increased O₂ exhaustion, in order to maintain a sufficient O₂ or energy status. The existence of this counter-regulation leads us also to expect, due to the average decrease in the resting $PO_{2\text{-art}}$ with age (Fig. 32), a consecutive age dependency of the resting $PO_{2\text{-ven}}$ which will ameliorate the effects of the severe

drop in the $PO_{2\text{-art}}$. And, indeed, reference [36] reports on a slight drop in the mixed central $PO_{2\text{-ven}}$ with increasing age.

In Fig. 58 the curve for the dependence of the mixed $PO_{2\text{-ven}}$ at rest on age according to [36] is drawn under the standard curve for the resting $PO_{2\text{-art}}$, already discussed. Despite the drop in the upper curve with age, the course of the lower curve surprisingly leads to a slight increase in the η -value with age. The fact that the O₂ status nevertheless significantly deteriorates with increasing age (see below) can be explained by the generally severe reduction in the cardiac output.



1.1.9.3 The increase in PO_{2-ven} due to stressful influences, particularly in conditions of weakness

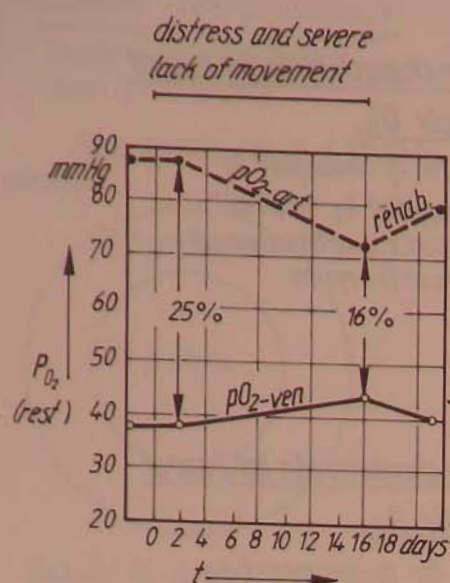
The strong dynamics of the resting PO_{2-ven} are very striking, and have a great influence on the utilization factor of the O_2 binding capacity of the blood, due to the great steepness of the O_2 dissociation curve in the area of the venous pressures. Examples of the course of PO_{2-ven} in lack of exercise, operation and in a phase with a 'flu infection are shown in Fig. 59. In all cases the η value sinks critically. The feeling of weakness in illness (energy deficiency), which forces the patient to stay in bed, correlates with the low η -values. The main contributor to the drop in η is the significant rise in the resting PO_{2-ven} , which has been observed in all cases so far. From the course of the PO_2 levels after the end of the 'flu infection, we can draw conclusions about the speed of rehabilitation.

The resting PO_{2-art} reducing effect of the very varied stressful influences which we discovered in [20, 21] and have commented upon in Paragraph 1.1.8.2, is reflected in the increase in the resting PO_{2-ven} . The O_2 transport to the body tissue is even more severely reduced by strong stressors than we had earlier suspected.

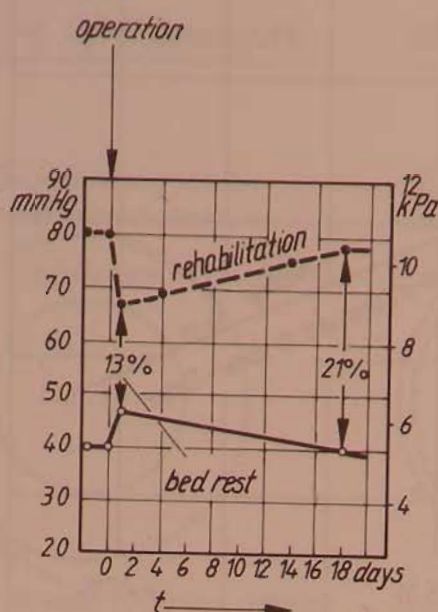
The great drop in the η -value in operations, due to general anesthesia, leads us to recommend the implementation of O_2MT before and after surgical interventions on older patients in order to reduce the risks [108].

Figure 60 shows an example, from the field of cancer therapy, of the worsening of the O_2 status due to the distress of chemotherapy, radiation therapy or surgery, which is still hardly known or taken into consideration.

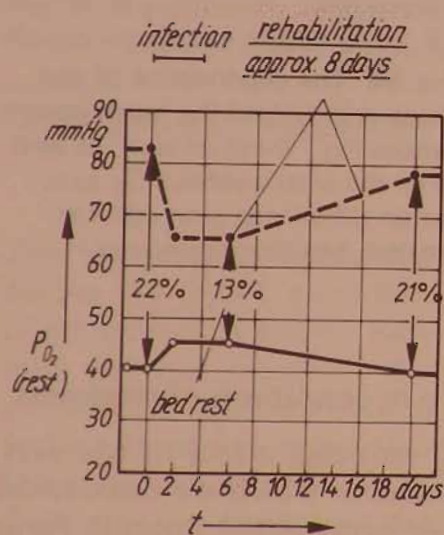
A Distress + lack of movement



B Operation, injury



C Influenza normal course



D Influenza

with quick rehabilitation

15 min

O_2 MT quick procedure

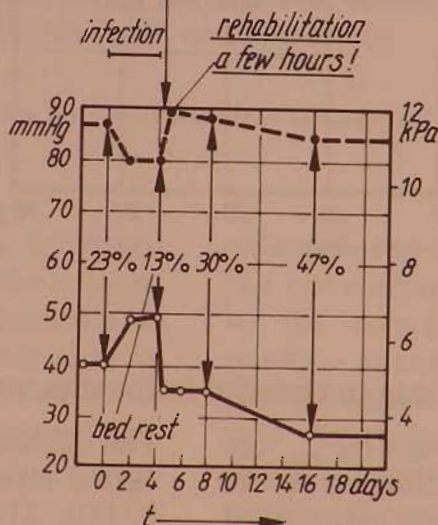


Fig. 59 Examples showing the decrease in the arterial, and the increase in the venous P_{O_2} (each at rest) by distress and severe lack of movement (A), operation (B) and influenza infection (C, D). η = utilization coefficient of the O_2 binding capacity of the blood

1.1.9.4 The reduction of $P_{O_{2-ven}}$ by means of O_2 MT procedures and exercise training

At the beginning of 1982 it was discovered [7] that a further basic effect of the 36 h O_2 MT procedure is a lasting drop in the resting $P_{O_{2-ven}}$. This drop, which normally contributes significantly to the increase in the η -value, is also very often observed, as already discussed above (Table 5), in persons in whom there was no lasting rise in the $P_{O_{2-art}}$. The mean drop in the resting $P_{O_{2-ven}}$ was 4.8 mmHg (0.64 kPa) in partial therapy responders and 6.2 mmHg (0.83 kPa) in partial nonresponders. In both cases there was an increase in the η -value to 150% of the starting value.

In a pilot study with larger numbers of subjects, the changes in the resting P_{O_2} levels after the 15 min O_2 MT quick procedure were in-

vestigated. The results of the P_{O_2} measurements after a single (first) application of this procedure in nonselected normal persons are summarized and statistically analysed in Table 6. On average there result an increase of 4.2 mmHg (0.6 kPa) in the resting $P_{O_{2-art}}$, a drop of 10.3 mmHg (1.4 kPa) in the resting $P_{O_{2-ven}}$ and an increase of 19% in the η -value from an absolute 28.2% before. The O_2 transport to the body tissue has therefore been increased by the single 15 min O_2 MT quick procedure to 164% of the starting level. The only slight variation of the $P_{O_{2-ven}}$ and the high statistical significance resulting from this are remarkable, as is the fact that this very strong effect, which can be used in many ways in

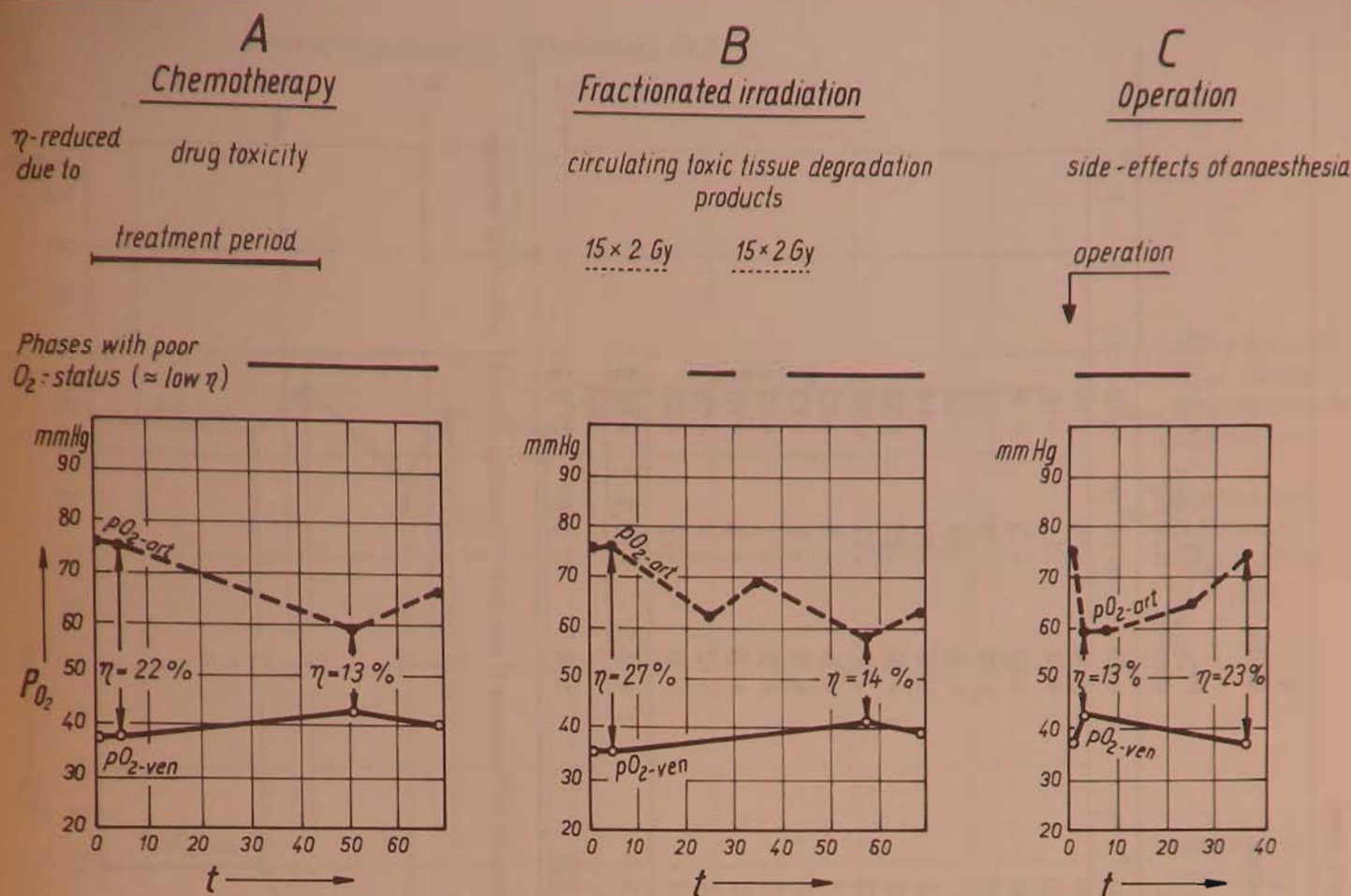


Fig. 60 Remarkable deterioration of the O_2 status (or of the η level as the main factor of O_2 transport to tissue) after cancer treatment by drugs (A), fractionated irradiation (B), or surgery (C); figures for orientation

medicine, in contrast to the quickly fading training effect, lasts a very long time (weeks to months and more). With between one and three applications of this quick procedure the average increase in the resting PO_{2-ort} is only roughly 1/3–2/3 of that attainable with the 36 h O_2 MT procedure. It is therefore recommended that the combination of both procedures be considered in cases where the PO_{2-ort} remains too low.

Figure 61 shows a test case of the improvement of the arterial and venous PO_2 values by means of the single and double repetition of the 15 min O_2 MT quick procedure. It can be seen that a single or a double repetition is worthwhile. This example and also those discussed below show the endurance of the treatment effects over the (arbitrary) observation time of 2–10 weeks.

In a self experiment, the external conditions and course of which are presented in Fig. 62, it was discovered that conditions of weakness of the organism are characterized by a fast and great increase in the resting PO_{2-ven} or drop in to close to the base value. The organism protects itself from damage (e.g. damage to organs) during this dangerous phase, by bedrest and a slight increase in cardiac output (pulse increase

from 60 to 66 per min in the example). The self experiments further showed that it is possible to eliminate the cause of the condition of weakness (i.e. O_2 deficiency) in less than 1 hour by means of the O_2 MT quick procedure. Under the very high, effective O_2 inhalation, a surprisingly high level of physical exertion, sufficient for the procedure, can be tolerated, despite the previous condition of weakness. The bioenergetic control of the capillary switching mechanism of the microcirculation (with a small time constant) is reflected negatively (distress) on the 3rd day of the experiment shown, i.e. "capillary narrowing", and positively, i.e. "capillary distension", on the 4th day at 11.50 a.m. (quick procedure).

Several (easily verifiable) findings about the immediate arrest of the consequences of distress of the type described in our figure, if the quick procedure is immediately implemented at the first symptoms, should develop into an important practical aid in future medicine.

A further typical result with a very similar course of the PO_2 and η -values is given in Fig. 63. In a 'flu infection with fever there is a severe increase in the resting PO_{2-ven} , and η approaches the base value. Once more the critically reduced value of η is normalized

Table 6 P_{O_2} measurements of unselected individuals, at rest, show the (lasting¹) increase in the arterial P_{O_2} and the statistically highly significant reduction in the venous P_{O_2} brought about by a single (first) treatment with the 15 min O_2 multistep quick procedure GK 2-I
 P_{O_2} measurement column 3 at least one day after end of process on the same arm (usually the right one)

1 Individuals			2 before 15 min O_2 multistep quick procedure			3 after 15 min O_2 multistep quick procedure			4 Difference		
No.	Age years	Sex ♂ ♀	P_{O_2-art} mmHg	P_{O_2-ven} mmHg	η %	P_{O_2-art} mmHg	P_{O_2-ven} mmHg	η %	P_{O_2-art} mmHg	P_{O_2-ven} mmHg	η %
1	75	♂	75	48	13 (flu)	84	34	32	+ 9	-14	+19
2	32	♂	84	50	12 (flu)	88	35	30	+ 4	-15	+18
3	65	♀	82	40	22	86	29	40	+ 4	-11	+18
4	63	♂	64	20	57	77	17	66	+13	- 3	+ 9
5	58	♀	64	22	52	84	18	64	+20	- 4	+12
6	70	♂	66	30	34	72	16	67	+ 6	-14	+33
7	45	♂	80	42	19	82	32	33	+ 2	-10	+14
8	46	♂	70	44	15	76	22	53	+ 6	-22	+38
9	71	♂	78	35	27	70	18	62	- 8	-17	+35
10	52	♀	80	30	37	75	25	47	- 5	- 5	+10
11	39	♂	79	32	33	84	26	46	+ 5	- 6	+13
12	58	♂	72	36	25	74	29	37	+ 2	- 7	+12
13	66	♂	71	34	27	74	26	45	+ 3	- 8	+18
14	58	♀	78	32	33	80	25	48	+ 2	- 7	+15
15	72	♂	64	40	17	64	28	37	0	-12	+20
15	58,0	N♂ N♀ =11 =4	73,8	35,7	28,7	78,0	25,3	47,1	+ 4,2	-10,3 ²	+18,9
	12,9		7,0	8,6	13,3	6,7	6,1	12,8	± 6,7	± 5,4	± 9,2

¹ The effect continues with a healthy lifestyle and disappears only after severe distress. This is a crucial difference from the "training effect", which is known to wear off after only about 2 days. (See also Fig. 44)

² $t_0 \triangleq$ statistical significance with a probability of error of 1%

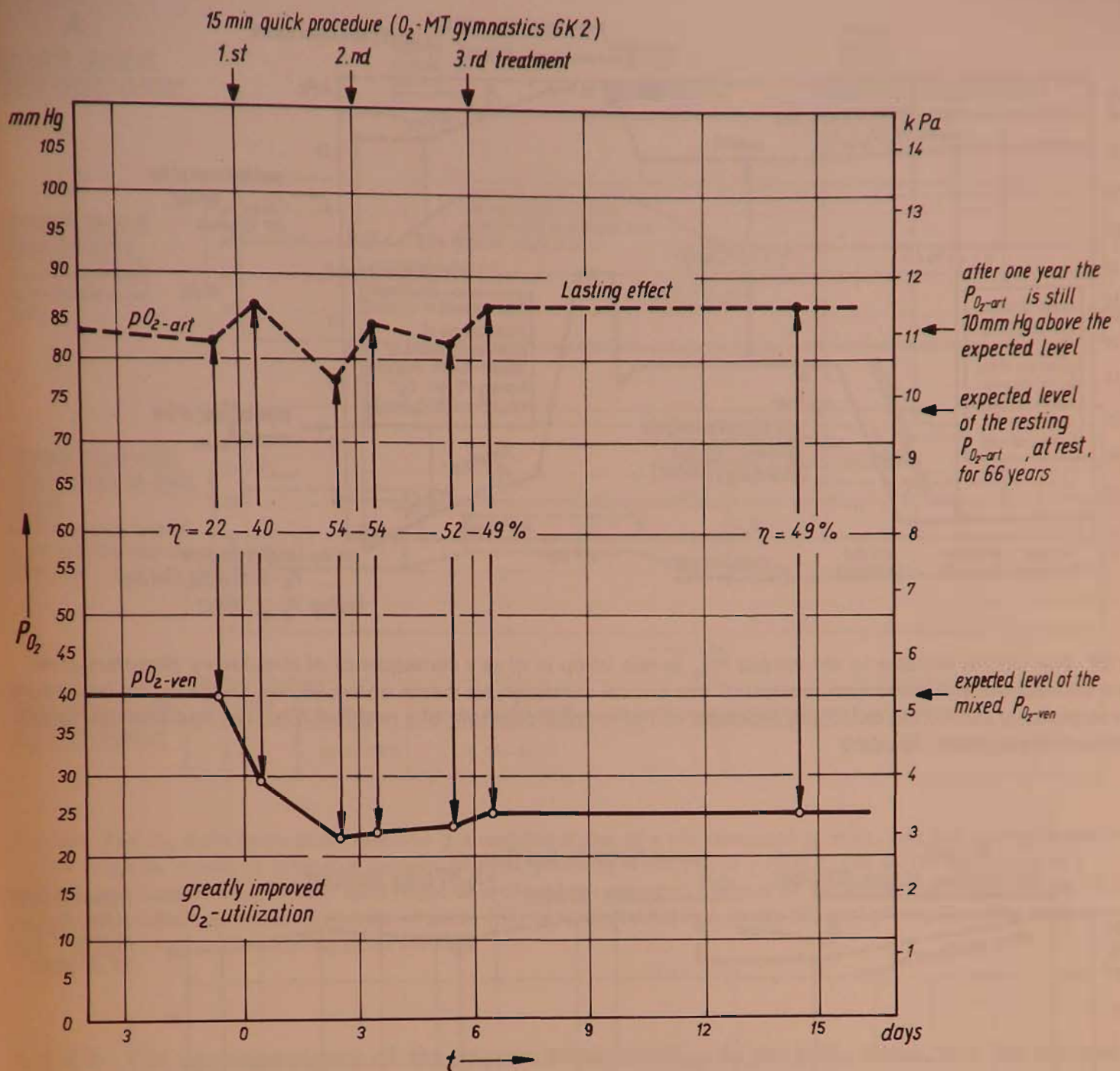


Fig. 61 Measurements of the (slight) increase in the P_{O_2-art} at rest, and the (great) drop in the peripheral P_{O_2-ven} at rest, by means of the 15 min O_2MT quick procedure with simultaneous physical strain. (Variant GK 2-I with bicycle ergometer 100 W, repeated twice) in a 66-yr-old female, treated roughly one year ago with the 36 h O_2MT . η = utilization coefficient of the O_2 binding capacity of the blood

within approximately 1 hour by means of the O_2MT quick procedure, and finally increased to three times the value. The measured values here document the *success of a fast rehabilitation after influenza*.

The effects detected on a patient undergoing combination treatment with the 36 h O_2MT procedure plus HOT*, which in January 1981 were at first attributed primarily to the HOT* procedure, are summarized and commented on in Fig. 64. In this example it is highly likely that the life of the over-90-year-old patient was prolonged by more than 2 1/2 years by the fast and lasting increase in the dangerously reduced η -value. The *increase in pulse*

occurring due to critical O_2 deficiency should always be seen as a *very serious warning signal* and taken as grounds for the implementation of an O_2MT variant suited to the physical performance capacity.

In measurements of the resting P_{O_2} before and after 3 weeks of stamina training (running), a lasting reduction in the P_{O_2-ven} (and increase in the η -value) was found as for O_2MT . Through *stamina training, too, the microcirculation is evidently high-charged long-term*.

Figure 65 shows a schematic presentation in which the main connections between the cellular capillary wall switching mechanism of the blood microcirculation and the various positive or negative influencing factors are summarized.

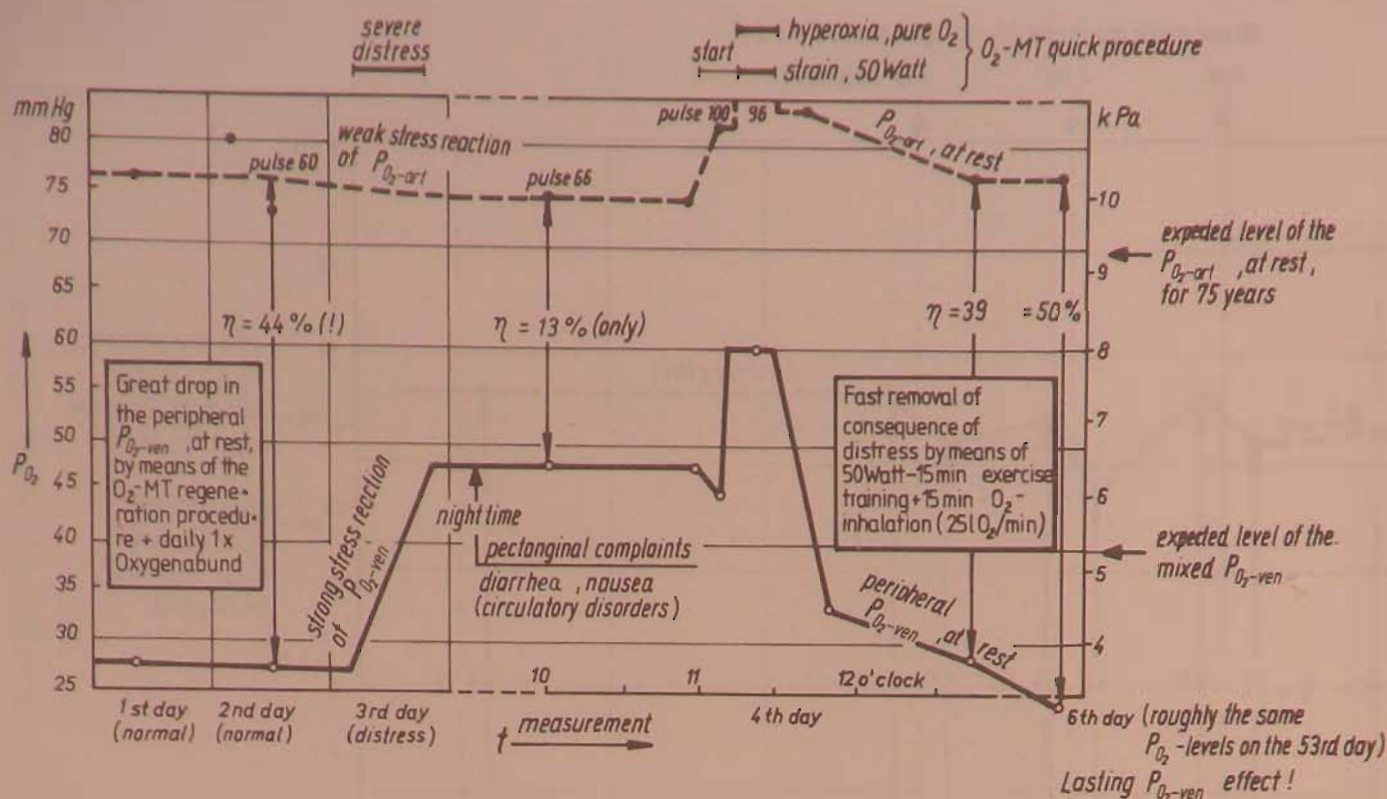


Fig. 62 The critical increase in the venous P_{O_2} at rest (drop in η) as a consequence of circulatory disorders after severe distress and the immediate reversal of this critical condition by means of the 15 min O_2 MT quick procedure. Bioenergetically controlled switching processes of the microcirculation, of a negative (distress) and positive (quick procedure) kind. Male, 75 years

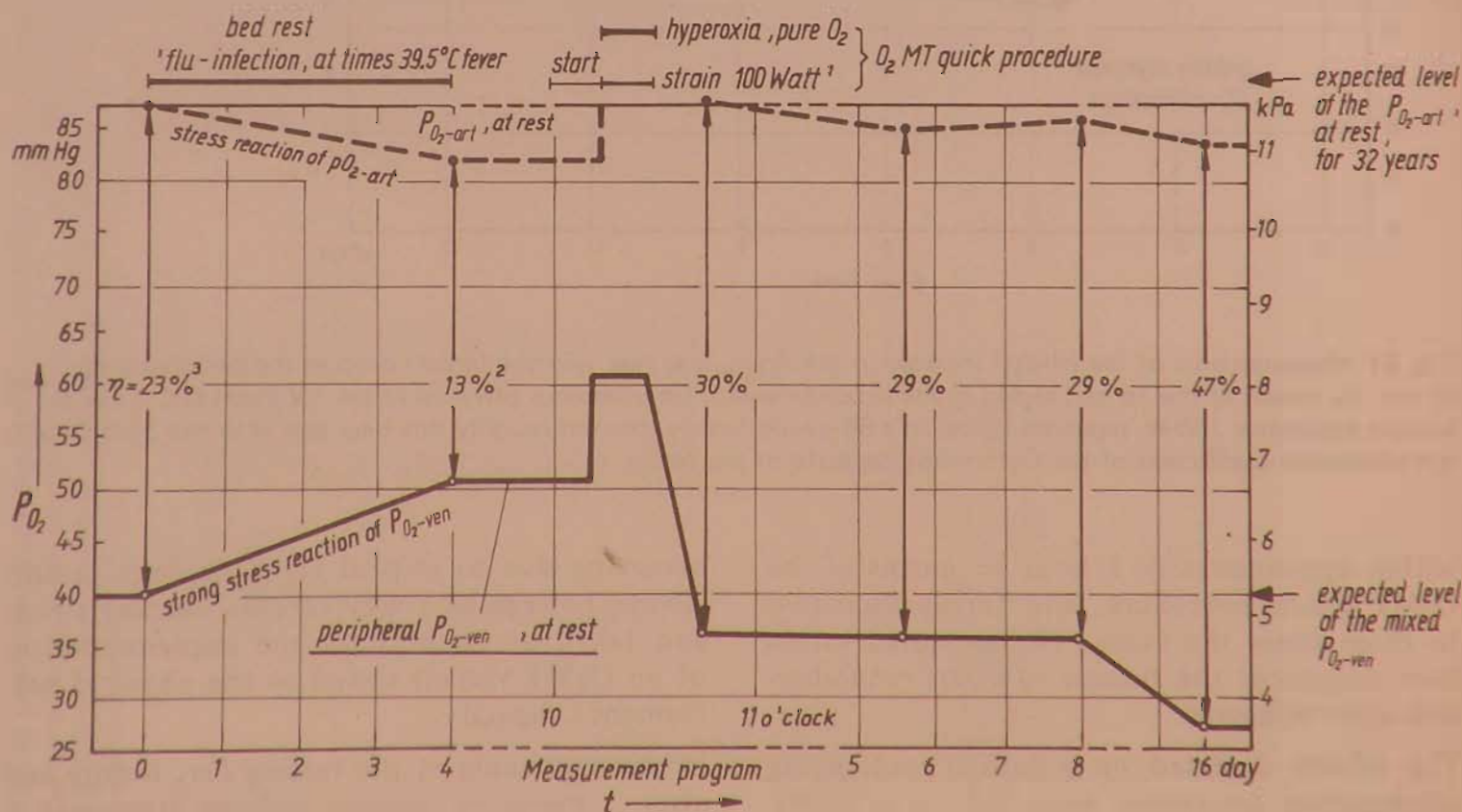


Fig. 63 Fast rehabilitation after a 'flu infection' by means of the 15 min O_2 MT quick procedure. Pronounced increase in venous P_{O_2} (critically reduced η level caused by 'flu infection'! Significant drop in venous P_{O_2} ; very high η level) caused by O_2 MT quick procedure. Lasting effect

¹ Bicycle ergometer (home trainer with watt display)

² It should be remembered that the P_{O_2-ven} measurement from the arm usually gives somewhat unfavorable (too high) values. According to our experience, the value of $\eta \cdot k_f$ should be 15–16% in this case

³ Empirical value for 32 years of age

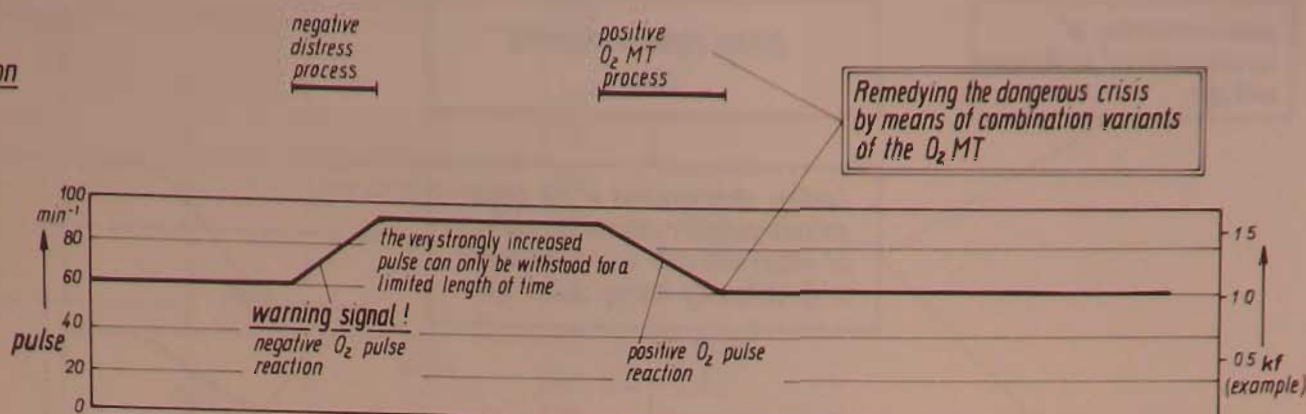
A

Energetic control of blood microcirculation

B

Temporal course of pulse frequency

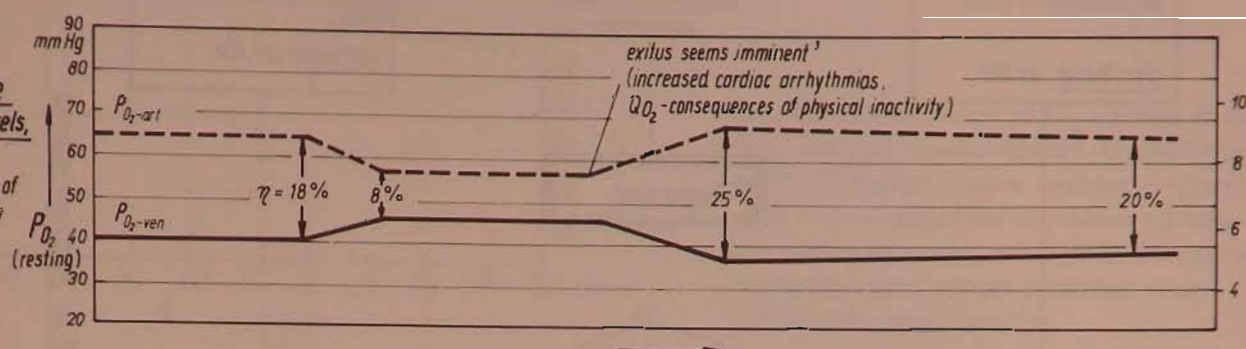
(roughly proportional to the cardiac output COP)



C

Temporal course of the arterio-venous pO_2 -levels, at rest

and of the resulting values of η , the O_2 -binding capacity of the blood



D

Course of the O_2 -offer Q_{O_2} to the organism

O_2 - status	normal for age 91 years	life - threateningly poor (dizziness, difficult breathing, total disablement)	normal, has so far lasted 16 months, prolongation of life and of high - quality life is to be expected
$\eta \cdot k_f$	$18 \cdot 1.0 = 18\%$	$8 \cdot 1.5 = 12\%$	$25 \cdot 1.0 = 25\%$ (March 1982)

Fig. 64 The O_2 deficiency pulse reaction is a warning signal of a life-threatening crisis, and the lasting remedying of the crisis by means of intensive variants of the O_2 MT (36 h procedure + HOT*, GK 4-111). Paradigm of a 93-year-old patient (May 1982) with negative and positive energetic control of the blood microcirculation (A) and with the correlating temporal courses of pulse (B), of both resting P_{O_2} levels (C) and of the O_2 offer to the organism (D). k_f = factor considering pulse increase

1.1.9.5 The age-dependency of the oxygen transport Q_{O_2} to the body tissue, and the increase in this transport by means of O_2 MT and exercise training

One characteristic of the older person is the drop in physical and mental powers with increasing age. Physically, the deterioration in the energetic status in the human organism lies behind this phenomenon. Since under normal conditions the energetic status is determined by the O_2 status, the curves of this status in Fig. 66 in their age dependency are of vital significance for everyone.

The dependence on age of the O_2 uptake and of the O_2 transport Q_{O_2} to the body tissue, determined under resting conditions each, was investigated in [37]. The result for normal untreated persons is shown in the lower curve (solid line) in Fig. 66. It can be seen that the O_2 transport, at rest, drops at an average age of 80 years to approximately 62% of the maximum at approximately 30 years. Figure 58 has already shown that the η -value improves with increasing age. The increase in η (mean in healthy volunteers) is entered numerically in

Fig. 67 A. The *real reason* why the oxygen or energy status usually deteriorates critically with increasing age, despite the increase in η , is the *reduction in cardiac output*. According to Fig. 67 B [109, 110], the cardiac output in normal persons of 80 years, who are inactive in accordance with their age, is reduced to roughly 60% of its maximum in youth. The difference in cardiac output between sportingly active, and inactive individuals is remarkable here. The age-dependent change in the product, $\eta \times$ cardiac output, which is largely decisive for the O_2 flow, is shown in Fig. 67 C.

Guidelines for the improvement which can be achieved with O_2 MT can be seen from the upper curve in Fig. 66, and from Fig. 68. It can be seen from Fig. 68 A that, in comparison to the η -value without treatment, there occurred in almost all age groups an approximate doubling of the η -value, and that there is a maximal increase in the age range from 50 to 80 years,

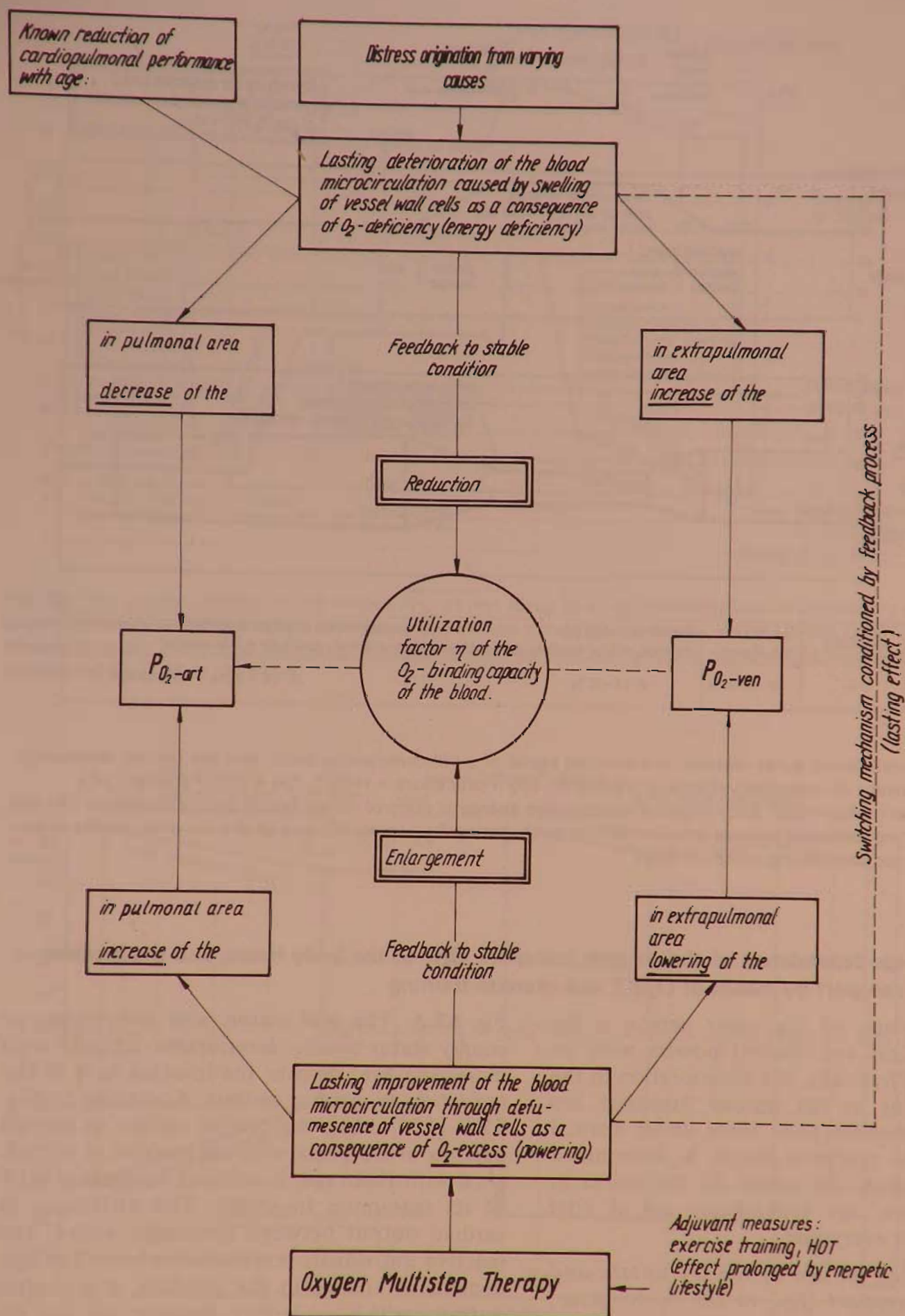


Fig. 65 Schematic presentation of the main connections between the cellular capillary wall switching mechanism and the positive/negative influences such as age etc. O_2 multistep therapy stamina training, distress

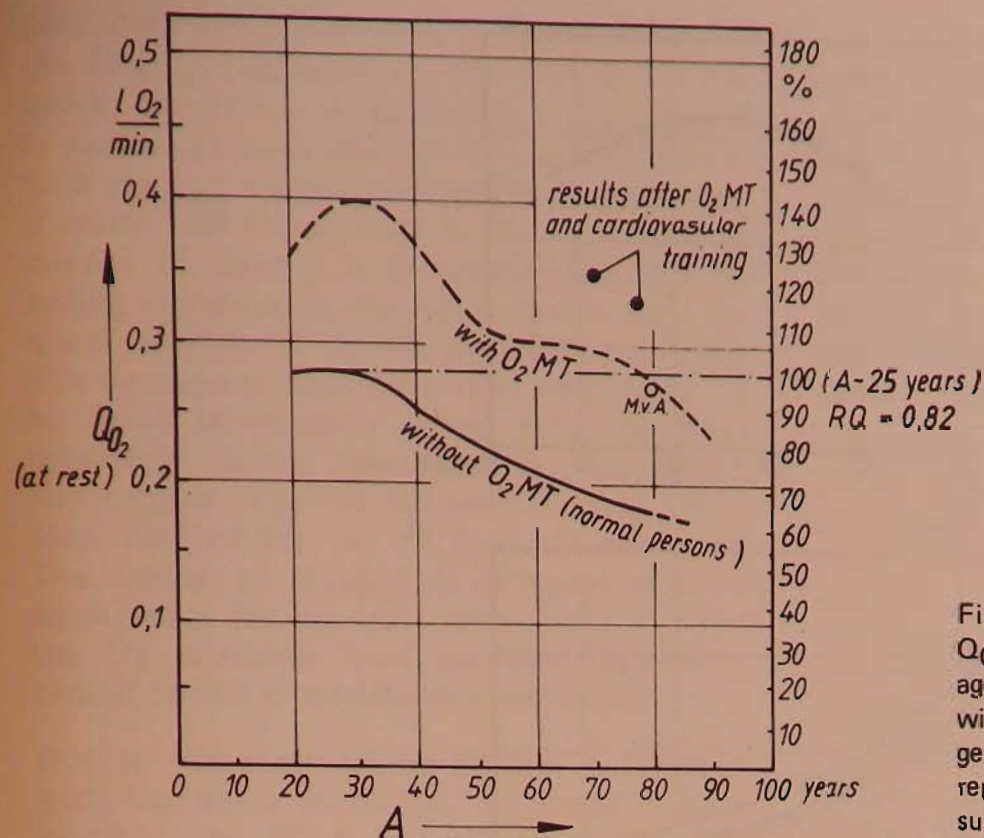
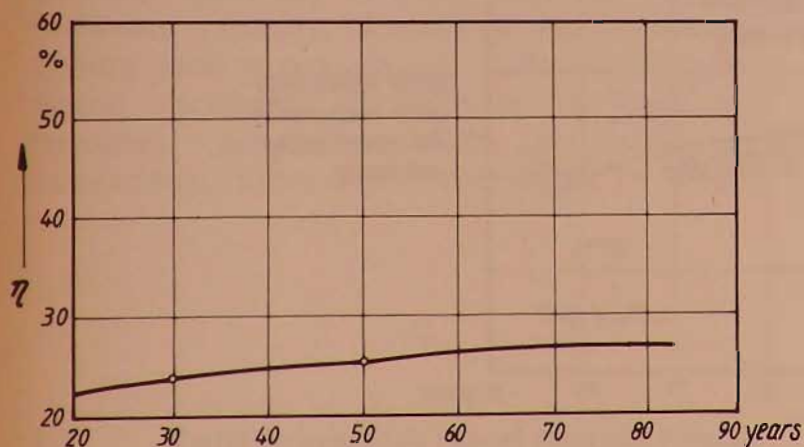
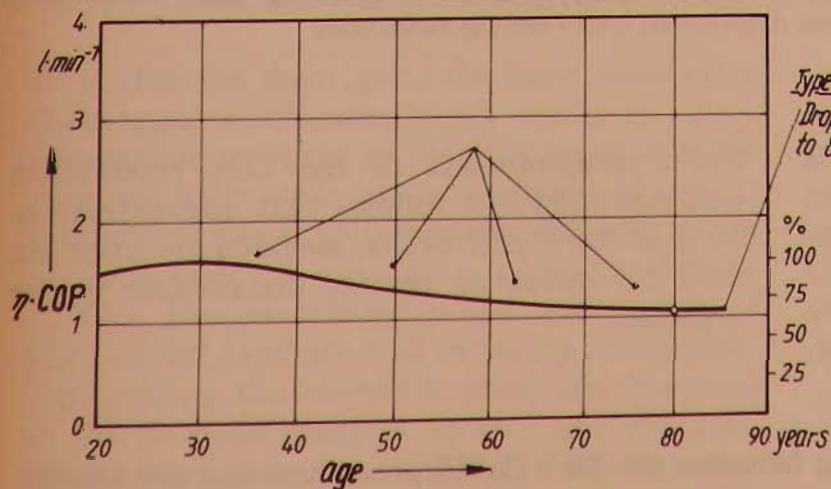
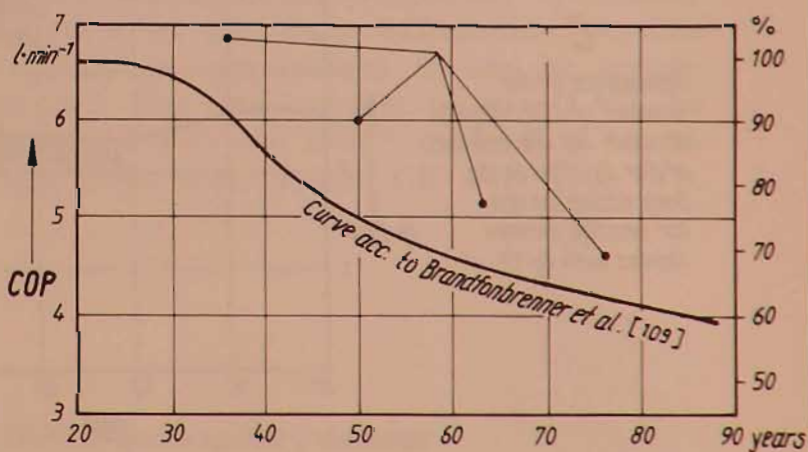


Fig. 66 Dependence of O_2 uptake at rest, Q_{O_2} (oxygen consumption in tissue) on age A of healthy males without (—) and with (---) permanently elevated oxygen status by means of O_2 MT. The curves represent mean values obtained from sufficiently large samples

A Dependence of the arteriovenous O_2 saturation difference on age in healthy, untreated persons (cf. Fig. 58)



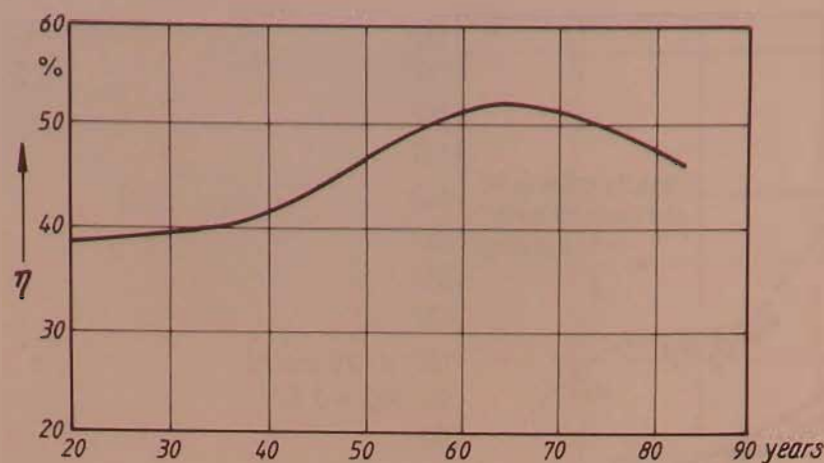
B Dependence of the cardiac output (COP) on age in healthy untreated persons



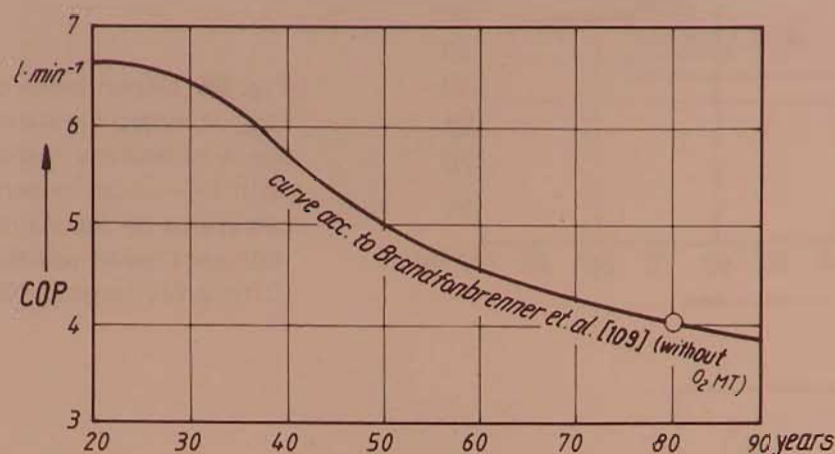
C Dependence of the product $\eta \cdot \text{COP}$, largely decisive for the volume of the O_2 flow to the body tissue, on age, for healthy, untreated persons

Fig. 67 The dependence of the arteriovenous saturation difference η (A), of cardiac output COP (B) and of the product $\eta \cdot \text{COP}$ largely decisive for the O_2 flow to the body tissue, on age, for healthy persons, not treated with O_2 MT. Mean levels from a large group of individuals. All values determined under resting conditions

A
Dependence of the
arteriovenous
 O_2 -saturation difference
on age in healthy persons
treated with O_2 MT



B
Dependence of the
cardiac output (COP),
on age in healthy persons
treated with O_2 MT



C
Dependence of the
product $\eta \cdot COP$, (largely
decisive for the volume
of the O_2 -flow to the
body tissue, on age,
for healthy persons
treated with O_2 MT

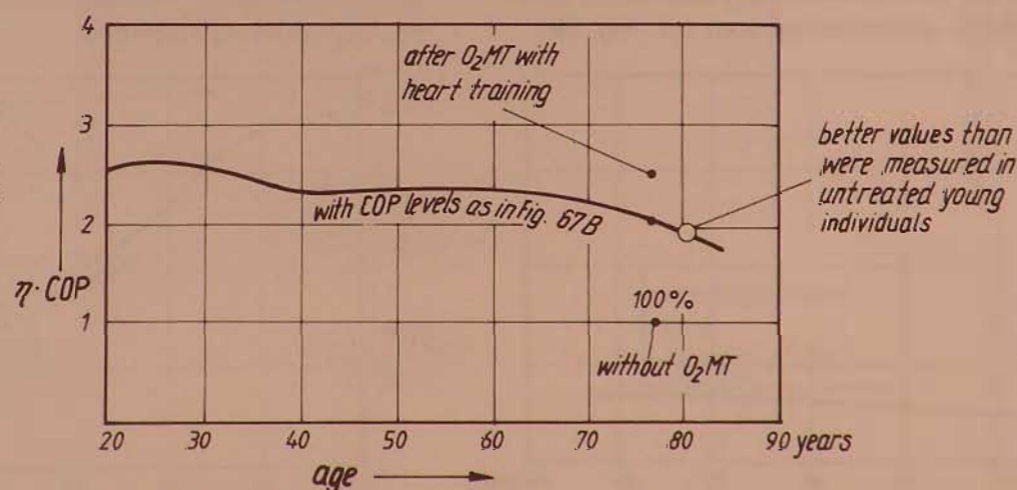


Fig. 68 The dependence of the arteriovenous saturation difference η (A), the cardiac output COP (B) and the product $\eta \cdot COP$ largely decisive for the O_2 flow to the body tissue, on age, for healthy persons after O_2 MT. Mean value from a sufficiently large group of individuals. All values determined under resting conditions

where an improvement in the O_2 status is particularly desired. If the curve according to Fig. 67 B is used as a basis for the age dependence of the cardiac output, then the curve for the age dependence of the O_2 flow to the body tissue in accordance with Fig. 68 C is obtained.

From measurements of the CO_2 production (see Appendix), it follows that approximately 50% of the O_2 MT-borne, elevated O_2 offer are used for increasing the O_2 metabolism in the organism.

1.1.10 Differences in effects and indications between the 36 h O_2 MT procedure and the 15 min O_2 MT quick procedure

From the total overview of our findings so far (cf. also Tables 5 and 6) it can be seen that the effect of the 36 h O_2 MT procedure lies some-

what more in the direction of an increase in PO_{2-art} (influence on the pulmonary function), and the effect of the single 15 min O_2 MT quick

procedure somewhat more in the reduction of the PO_{2-ven} (influence on O_2 utilization). The quick procedure is particularly indicated in (younger) persons (subjected to severe distress) with PO_{2-ven} levels ≈ 40 mmHg. Furthermore, it seems that the increase in PO_{2-ven} as a consequence of distress is so pronounced that the lasting elevation in this value makes more frequent repetitions of the procedure necessary. The decision to undertake such repetitions can be much more easily taken with the quick procedure, as the *time (also for the patient) and oxygen required are only roughly 5% of that required for the 36 h O_2 MT procedure.* The saving of oxygen is of great practical significance for all areas and countries where the O_2 provision from pressure cylinders or central facilities constitutes a bottleneck.

Due to the great savings in time and oxygen with the quick procedure, the question arises whether the 36 h procedure can be fully replaced by it. This question must be answered in the negative and not only due to the somewhat different effects discussed. *The 36 h O_2 MT procedure will be specifically indicated, in the future also, for patients with restricted mobility* (cardially or pulmonally limited performance capacity, diseases of the locomotor system such as coxarthrosis, gonarthrosis, peripheral circulatory disorders in the lower extremities, conditions after amputation of extremities, pronounced conditions of weak-

ness, severe hypertension and other diseases being incompatible with the application of the quick procedure). The 36 h procedure with its supply of oxygen via the comfortable mask applicator will also be preferred in cases of respiratory insufficiencies (advanced lung emphysema, bronchial asthma, lung fibrosis, chronic bronchitis, conditions after pneumothorax), also in cases of limited psychic stress capacity (claustrophobia etc.).

The 15 min O_2 MT quick procedure GK 2-I, to be repeated once or twice, if necessary, is indicated for sufficiently able-bodied persons (elimination of acute conditions of weakness in younger and older persons, especially after operations, infectious diseases, accidents and other stressful events; further, to increase the physical performance capacity before stress of all types, like operations and particular physical strains, amelioration of jet-lag in journeys from east to west etc.). The use of the quick procedure has great possibilities in outpatient departments. For sufficiently able-bodied patients without much time, the 5 x 20 min O_2 MT cure procedure GK 9-I (see Appendix) has been developed.

In extreme situations (e.g. severe circulatory disorders in the lower extremities, possible necessity of amputation) it can be recommended that the variants of the O_2 MT be combined with the HOT* method, as has already been done (variant GK 4-III, [50, 74]).

1.2 Total irreversible blood microcirculation inhibition and capillary damage

1.2.1 Ideas about and investigations into the mechanism of the total capillary occlusion

It is, for the most part, the same elementary rheological mechanism which causes the *total, irreversible stoppage of the blood microcirculation and afterwards capillary damage*, in cardiac infarction, shock, inflammation and also in the modern concept of cancer multistep therapy (CMT). This mechanism is the continuation of the cellular capillary wall switching mechanism, representing the reversible phase and discussed in the previous chapters, to an irreversible end. The difference in the triggering of the mechanism consists mainly in the fact that the O_2 deficiency-conditioned endothelial swelling and the reduction of blood flow are accompanied by a considerable pH reduction; this pH drop is

caused by a stronger or weaker transition to fermentation metabolism in the tissue surrounding the capillaries, and by the hampering of the drainage of the lactic acid formed. In this process pH levels of ≈ 6.6 can occur at the venous end of the capillaries, leading after a latent period to hemostasis.

This pH reduction causes a rearrangement in *the architecture of the biomembranes* [112]. This alteration in the membranes affects the microcirculation synergistically in many ways because, according to Table 7, changes occur, both in the blood cells and in the inner surface of the endothelium, which impede the microcirculation. Flexibility is critically

Table 7 The change in the architecture of bio-membranes as a pH-sensitive basic process for the multi-functional, extremely pH-sensitive stop of microcirculation, plasma leakage in capillaries at low pH, red cell aggregation (see Fig. 75)

Basic process	Elements involved in the starting process	1. Effects 2. Additional influences	Overall effect
1. Change in the architecture of bio-membranes during the transition from the normal pH = 7.4 to the value pH = 6.5 ¹ Findings of physical analysis (Kreutz, Hoelzl-Wallach, Freiburg 14.9.1976)	1.1 Erythrocytes	Great reduction of flexibility	The combination of and interactions between these strongly pH-dependent and blood flow-reducing effects finally condition the pH-sensitive stop in microcirculation
	1.2 Leucocytes	Reduced flexibility, adhesion to the venular endothelium; jamming of erythrocytes	
	1.3 Platelets	Increased formation of microthrombi	
	1.4 Surface layers Endothelium Fibrinogen	Increased stickiness, non-enzymatic adhesion of fibrinogen to endothelium	
2. Additional factors for the selective triggering of the irreversible stop of blood microcirculation in the cancer tissues	2.1 Blood picture	Number of leucocytes and thrombocytes normal or (artificially) increased	(Support)
	2.2 Blood flow	When blood flow is reduced, influx of leucocytes into the capillaries is greatly increased (timing!)	Adjuvant influence
	2.3 Endothelial swelling	Narrowing of the capillaries when there is O ₂ deficiency, especially at hyperthermia, decreased blood flow and shear stress	Prerequisite

¹ Additional pH drop in the capillary-venule area when microcirculation is greatly reduced by hampered lactic acid drainage (feedback mechanism)

the red cells and leucocytes. The measurement given in Fig. 69 proves this of the red cells [113, 114]. It follows from these measurements that, even at pH 6.5, there occurs a total stiffening of the red cell membranes and thereby also a *loss in red cell flexibility* [113–116]. The stiffening of the leucocyte membrane also has severe consequences. As can be seen very clearly using a vital microscope, it leads to a slowing down of the flow in the capillaries and to a jamming of the red cells with the leucocytes. A pre-stage of capillary damage looms (see [117] for observations of processes of this type in the terminal network with the scanning electron microscope). The subsequent process of the pressing of leucocytes against the venule wall in the capillary/post-

capillary transition zone by accumulated (stiffened) red cells which overtake the leucocytes there has been investigated in [118]. Fractions of a second (at pH $\approx$ 6.5), in which the blood cells pass along the venous part of a capillary, are sufficient to trigger the alteration of the red cell membranes. The alteration of the membrane structure and the formation of pores are reversible [119]. This means that a *grossly impeded microcirculation can be brought back to normal flow by increasing the pH of the venous capillary blood* (e.g. by means of a quick elimination of the O₂ deficiency which suppresses glycolysis, or by rapid administration of g-strophanthin, which re-normalizes the pH in the myocardium).

(Laser-Raman Spectroscopy)

Hoelzl-Wallach USA
cell membrane structure
modified normal

venous capillary end
in tissue with O₂-deficiency

O₂-deficiency
confluence

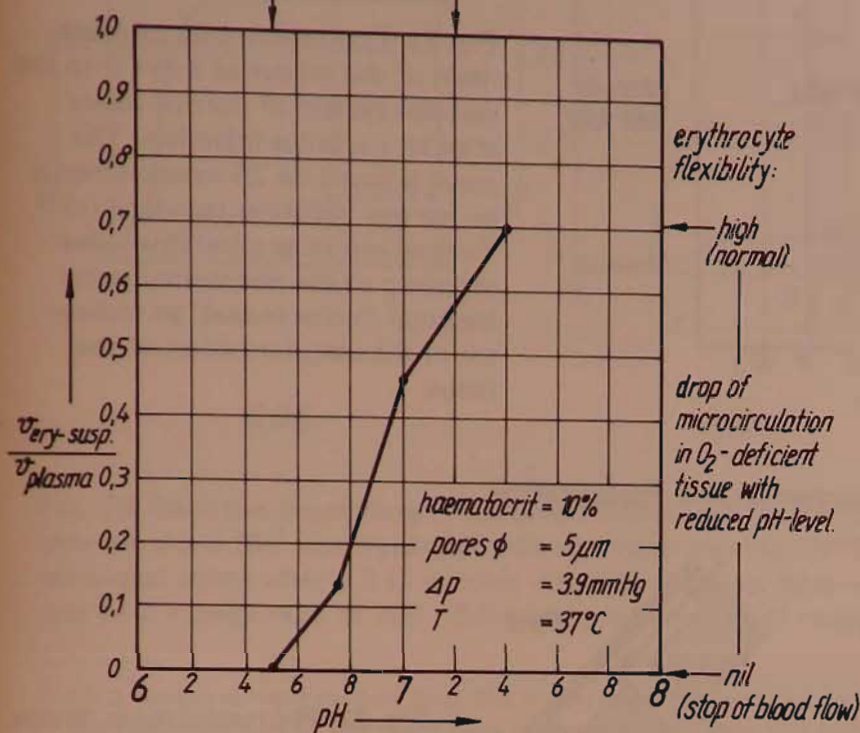


Fig. 69 Disappearance of erythrocyte flexibility at pH $\approx$ 6.5. Measurements of the relative flow rate of a red cell suspension as compared to plasma through pores with 5 μ m ϕ . H. Schmid-Schönbein et al. [114, 115]

¹ cf. also W. Kreutz, Freiburg/Br. FRG. Colloquium M. v. Ardenne on 14.9.1976 in Freiburg in the Institute of Biophysics and Radiation Biology of the University

A. Capillary in normal tissue

pores (85)	ϕ nm	d chink nm	molecule passage to H ₂ O	ΣF as proportion of surface
small pores	1	5	35 000	$\approx 10^{-3}$
large pores	24-70		500 000 (basal membrane)	$\approx 10^{-6}$

B. Capillary in tissue areas with longer lasting O₂-deficiency

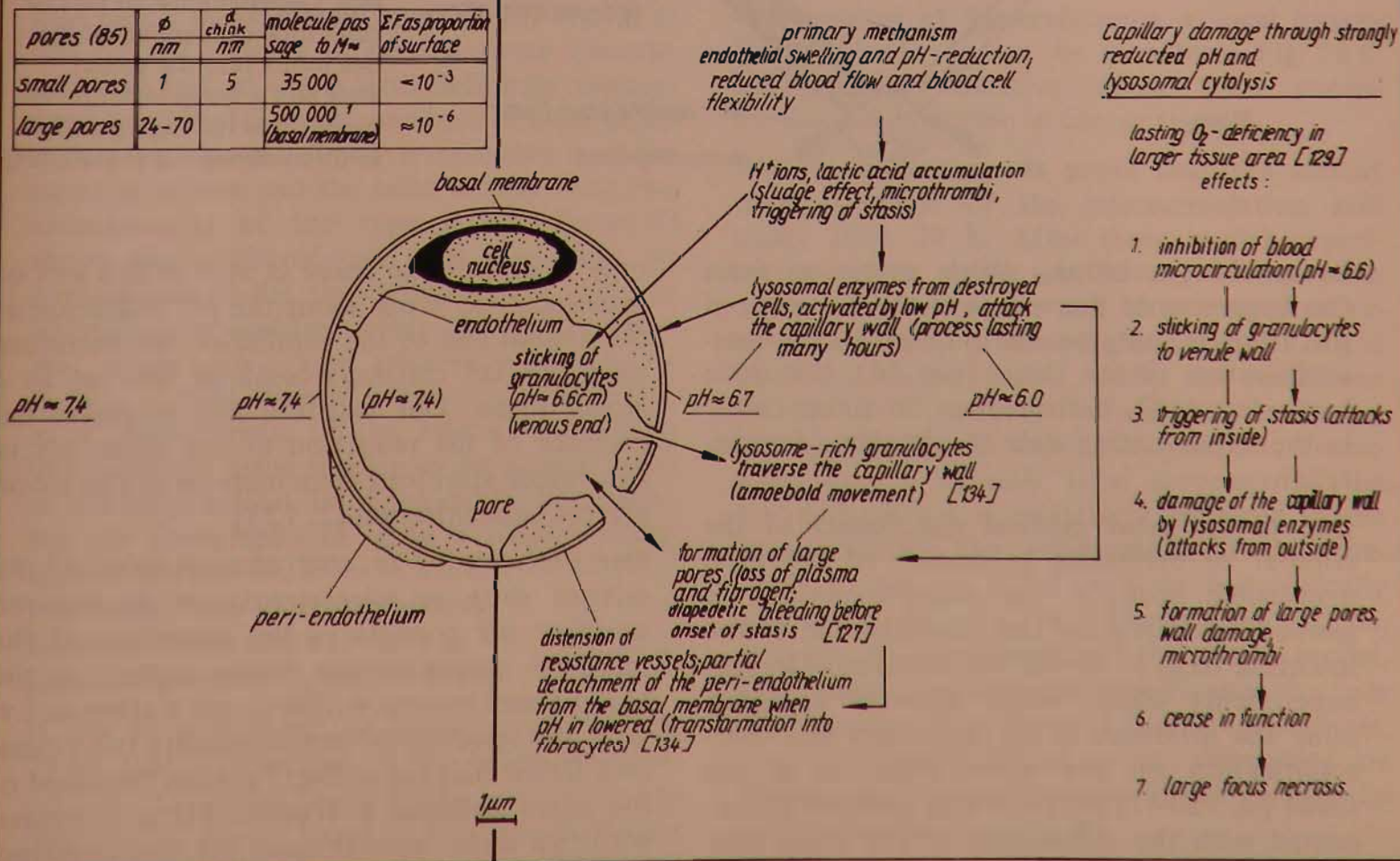


Fig. 70 Cross-section of a capillary (A) and postulated processes in capillary damage in a long-term O₂ deficient

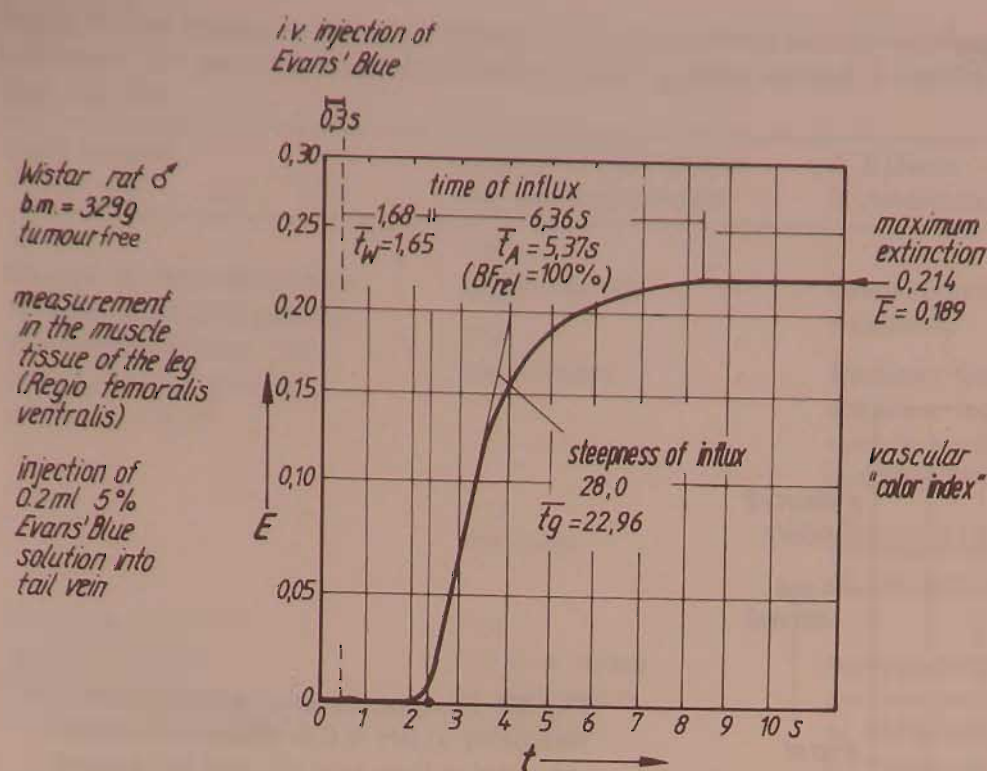


Fig. 71 Photoelectric measurement of the inflow of a dye into the vascular system of normal tissue after an i.v. bolus injection. The curve is based on 20 measurements on normal tissues as standard [121]. Time of influx as a (relative) characteristic of the microcirculation. Vascular "color index" an indicator of the vascularization of the tissue

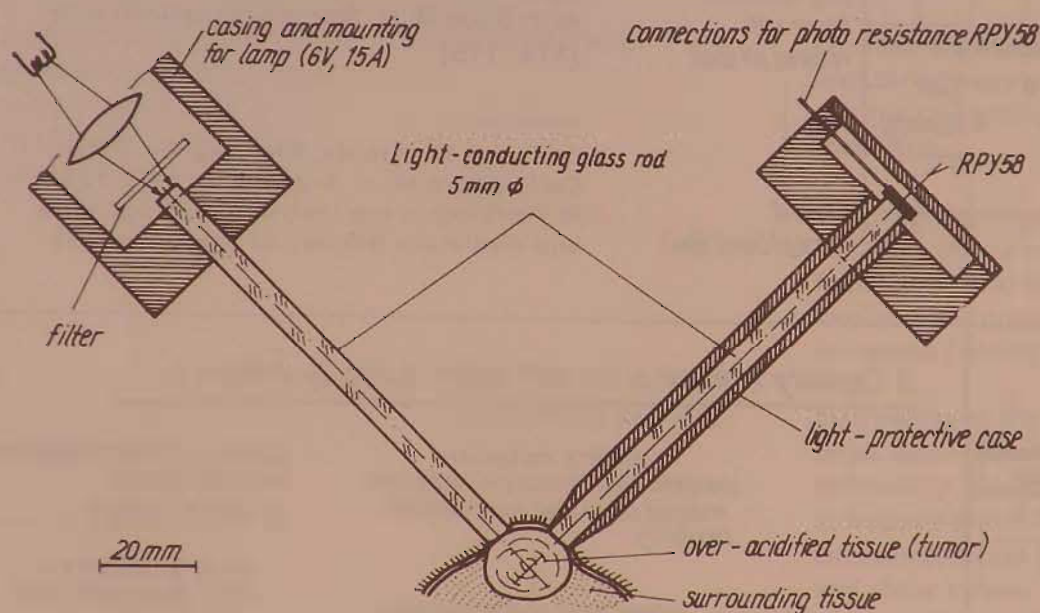


Fig. 72 Photoelectronic device for measuring relative blood microcirculation of tissues in situ at different pH values and with or without hyperthermia. Determination of sort of color index (steepness of the dye influx into the tissue) after an i.v. bolus injection of Evans' Blue (50 mg/kg as 5% solution during 0.3 s) [120, 121]

Irreversible occlusion, which progresses from the beginning of the venule in the direction of the arteriole, only occurs in longer-lasting over-acidification of the tissue (Fig. 70), that is, in longer-lasting O_2 deficiency or, in cancer tissue, in the longer-lasting state of stimulated fermentation.

Due to the great medical significance of the combat or deliberate generation of the total irreversible stop in the microcirculation, it seemed necessary for the strengthening of the scientific basis to devise and implement in vivo experiments which would allow us to determine the influence of O_2 deficiency and over-acidification on the microcirculation in the tissue [2, 120–123]. Since this problem is concerned with the influencing of the blood flow by means of pH reduction within the capillaries and venules, it is, in principle, irrelevant which

type of glycolysing tissue is used in this sort of experiment to bring about the pH reduction at the venous end of the capillaries. We therefore used the DS carcinosarcoma of the rat as a *model tissue*. Our Institute had extensive experience of the reduction of the tissue pH in this tumor after long-term increase of the blood glucose concentration [2, 123].

Our principle of in vivo measurement of the relative drop in microcirculation at reduced capillary pH consists in the recording of the temporal course of the "color index" in the blood vessel system within 0–60 s after an i.v. vital dye injection of approximately 0.3 s duration (Evans Blue) as in Fig. 71; then the slope of the curve obtained at reduced pH is compared with that under normal tissue pH. The construction of the optical wave-guide arrangement developed for this is presented in Fig. 72. With

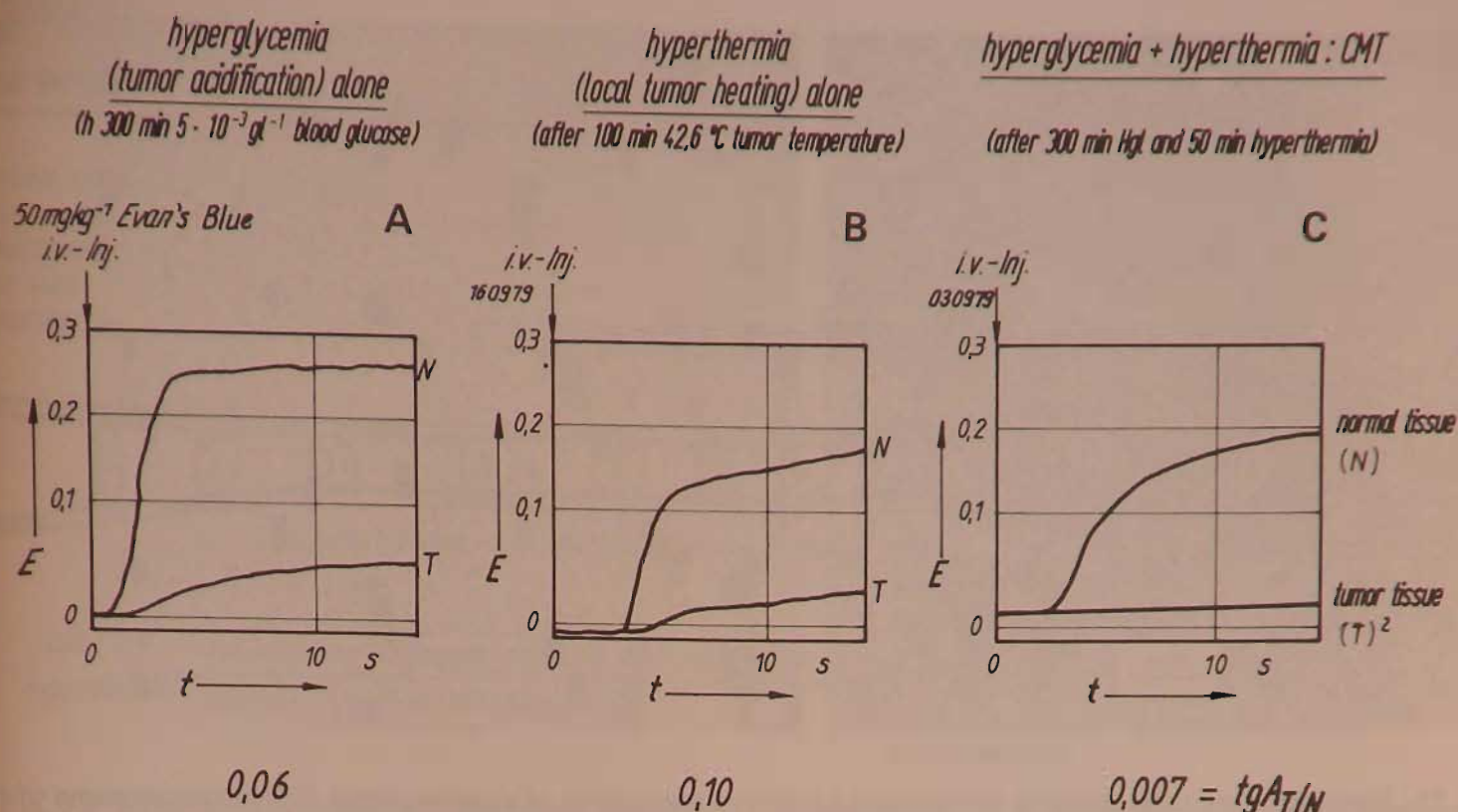


Fig. 73 Selective staunching of the blood microcirculation in cancer tissue after hyperglycemia alone (A), hyperthermia alone (B)¹ and hyperglycemia and hyperthermia: CMT (C). Photoelectronic simultaneous recording of the intravasal influx after 0.3 s i.v. bolus injection of Evans' Blue in normal tissue (N) and in tumor tissue (T). Wistar rats with a body mass of 200–250 g and a tumor mass of roughly 7 g

¹ This measurement reveals that the hyperthermia step also causes a selective microcirculation inhibition, as the microcirculation in normal tissue remains at virtually the same level

² Same picture after 24 h

this quick measurement method the course of the optical density in normal tissue (muscle, one leg) and in tissue with definitely reduced capillary pH (DS carcinosarcoma in hyperglycemia, contralateral limb) is recorded simultaneously in one and the same animal using two arrangements of the type shown. Figure 73 shows the results of such twin recordings. By comparison of the slopes of the dye influx in strongly over-acidified tissue tgA_T and in normal tissue tgA_N one obtains $tgA_T/tgA_N = tgA_{T/N} = TMI$ (tumor microcirculation index) as a characteristic of the microcirculation in overacidified tissue relative to the normal tissue of the same animal. In our example (Fig. 73 A), the pH topography of curve T roughly corresponds to the conditions in a severe myocardial infarction; the microcirculation in the over-acidified tissue sinks to $tgA_{T/N} \approx 6 \cdot 10^{-2}$ (triggering of extreme O_2 deficiency).

It can be seen from the further example (Fig. 73 B) that a reduction in the blood microcirculation to similar levels ($tgA_{T/N} \approx 10^{-1}$) was observed in cancer tissue in local hyperthermia alone, i.e. without hyperglycemia. Only our

combination of hyperglycemia + local hyperthermia leads, as can be seen from Fig. 73 C [121], to the selective, almost total, microcirculation inhibition in cancer tissue.

Further measurements prove that the almost total stoppage of the microcirculation still exists after 24 h. After these model experiments, which could also be reproduced with other types of tumor, and after analogous experiments with further adjuvant steps [124], it could be estimated that, under the conditions of the 1977 concept of cancer multistep therapy [125], the described complex mechanism with a virtually total stoppage of the microcirculation is selectively triggered in the cancer tissue. The achievement of this irreversible stop in blood flow is histologically confirmed by Fig. 74. These observations, relevant for this animal and this tumor model, have gained fundamental significance for our CMT concept. As a result of clinical experiences, however, modifications occur, depending on therapy management, tumor histology, vascular architecture and host tissue.

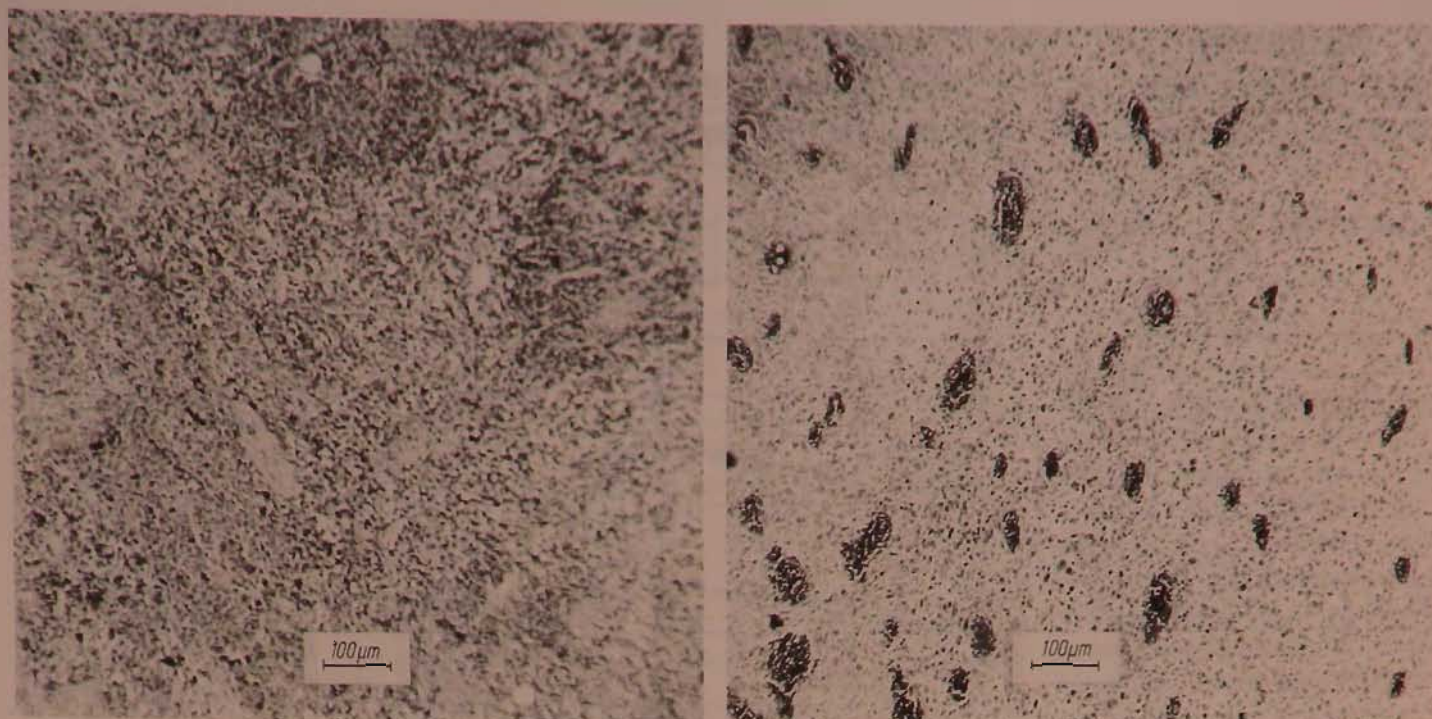


Fig. 74 Histological pictures showing the successful selective segregation of a cancer tissue (DS carcinosarcoma of rat) from the circulation through uniform triggering of irreversible hemostasis with the aid of extreme overacidification + 42.5 °C local hyperthermia and further measures of the cancer multistep therapy concept. The blood vessels are expanded and obstructed (B) (trichrome staining according to Goldner, green filter)

1.2.2 Cancer multistep therapy (CMT) and oxygen multistep therapy (O₂MT)

The central therapeutic mechanism in the CMT is the *selective irreversible closure of the vessels of the tumor* growing in the body [22, 23, 129]. This new method, used by us clinically with success for the first time in 1979, is fascinating for many reasons because:

1. due to the vascular obstruction, a segregation of the cancer tissue from the circulation of the organism occurs; thus the toxic strain on the circulation due to the sudden inundation by tumor degradation products is eliminated and at the same time the danger of internal bleeding is reduced.
2. the direct therapy target is not only formed by the cancer cells with their enormous variation in cell kinetic parameters, but additionally and mainly by the blood and vessel wall cells with their greater uniformity.
3. there exists justified hope that a universal therapy principle will be achieved, with individual arrangements in terms of tumor histology, vessel architecture, host tissue, stage and localization of the tumor, as all solid tumors are nourished via the blood vessels and must perish when these vessels are obstructed.

It is understandable that our ideas about the mechanism of capillary/post-capillary vascular occlusion have developed particularly from our

CMT research. Figure 75 gives a summary of the new ideas developed in close co-operation with P.G. Reitnauer. We know today that both the formation of pores and the aggregation of red cells are favored by pH reduction. Compared with the course of the same mechanism in myocardial infarction or inflammation [30] for example, the difference in CMT lies in the fact that the adjuvant step of local hyperthermia of 42–43 °C is necessary for the triggering of hemostasis, and to enable the contribution of endothelial swelling and red cell aggregation to become fully effective. This is obviously a specific characteristic of the cancer tissue capillaries (known to be previously dilated).

In our research to optimize the selective vascular occlusion, many series of experiments were carried out, partly also on the basis of suggestions kindly given to us by numerous colleagues. None of these efforts met with radical success. One idea presented itself at the beginning of 1982 from the O₂MT research, with the discovery of the bioenergetically controlled cellular wall switching mechanism, and from vital-microscopic investigations: there resulted, as a concrete measure to increase the probability of occlusion, the idea of *interrupting O₂ inhalation for a time at the start of the local or regional hyperthermia phase*, in order to promote, by a temporary drop in the O₂ off-

advanced stage
arterial vessel
expanded and
gorged with
erythrocytes

with 42°C and
 O_2 -deficiency

swelling of the endothelial cells (reduced
diameter)

extravasation of fluid increasing with time (pore formation)

deformation zone ← erythrocyte → stiffening zone

sluggish flow
erythrocyte aggregation

leucocyte
irreversible hemostasis

$\text{pH} = 7.4$ hyperthermia
pH-reduction increased tendency to wards aggregation
increase in apparent blood viscosity.

$\text{pH} \leq 6.7$

increased hemostasis

Fig. 75 Schematically presented ideas about the triggering of the mechanism of blood microcirculation inhibition in longer-lasting strong tissue overacidification (and hyperthermia). Examples: myocardiac infarct, inflammation, gangrene. Manipulated selective hemostasis in cancer multistep therapy (CMT) with two-step regional hyperthermia (selectotherm process)

the endothelial swelling discussed in detail [127, 128, 134]; there also resulted the instruction temporarily to increase the blood glucose concentration as much as possible (to eight times its normal level) in order to optimize the selective pH reduction in the cancer tissue. Along the same lines lay the measure of the *temporary blood flow strapping* [124], inasmuch as access to the arterial arm of the tumor concerned was possible. Other measures have recently been added in order to stimulate the selective extravasation of fluids, and the red cell aggregation in the vascular network of the tumor, corresponding to the ideas in Fig. 75 [130].

The measurement of red cell aggregation was pioneered by H. Schmid-Schönbein [131], Chmiel [132] and Reitnauer (influence of pH) [133].

The other condition for the selective triggering of the vascular obstruction in the cancer tissue is that, for 100–200 min, a *local temperature of around 42.5°C* is attained in the tumor, but even better than this, in the *region of the body* where cancer tissue is suspected (combat of metastases). In order to fulfil this condition in the human organism, the *CMT Selectotherm procedure* was devised, in which for the first time a very homogeneous energy supply to a large volume of tissue is achieved by means of the scanning movement of the applicator, fed by a short-wave transmitter. The principle of this procedure stems from Fig. 76 [135–139]. This procedure uses the *basic principle of two-*

step hyperthermia, already suggested in 1965 [2]. According to this principle, the first step attains a whole body temperature of, e.g. 41°C , and the second step adds to this further temperature increase of $1.5\text{--}2.0^{\circ}\text{C}$ for the part of the body where cancer is suspected, by means of regional hyperthermia.

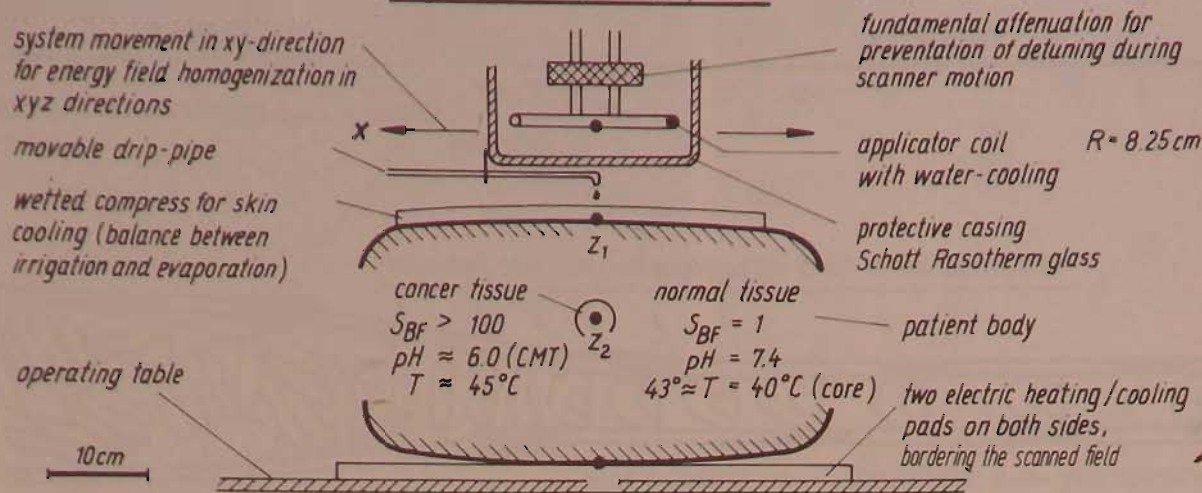
Thanks to this two-step principle, the necessary temperature span of the regional hyperthermia and of the temperature gradient is greatly reduced in a vertical direction to the body surface, and hence the danger of thermal damage to normal tissue near the skin is considerably reduced.

In order to save the expensive high-frequency energy which had until now been used to increase the body temperature to, e.g. 41°C , a Selectotherm variant was created with which the whole-body heating of the patient occurs by infrared A radiation, in accordance with Fig. 77 (also suitable for variable body sections).

Figure 78 shows a schematic presentation of the *CMT Selectotherm equipment of the 3rd generation*. This equipment makes possible, by control of the applicator "orbits" with the robot system (Fig. 79), the adjustment of the desired scanning and thereby the *adaptation of the regional energy supply to the individual treatment case*.

By means of the development of new applicator

CMT Selectotherm equipment



data: RF transmitter
 $N = 1.5 \text{ to } 8 \text{ kW}$
 $f = 27.12 \pm 6.0 \text{ MHz}$
 $\lambda = 11.06 \text{ m}$

scanning
 $x \text{ period} = 10 \text{ min}^{-1}$
 $y \text{ period} = 0.5 \text{ min}^{-1}$
 $v = \text{e.g. const.}$
 amplitudes = e.g. $\pm 20 \text{ cm}$

Fig. 76 Selective CMT scanning hyperthermia according to M. and Th. v. Ardenne. Selectotherm equipment of the 1st generation. Scheme of the decawave magnetic field arrangement for homogenous energy deposition in a large tissue volume for the selective high temperature rise in the overacidified cancer tissues. Guiding values. Through the meander-like movement of the coil system in xy-direction, for the first time a relatively homogenous energy deposition is attained, even to deep-seated tumors

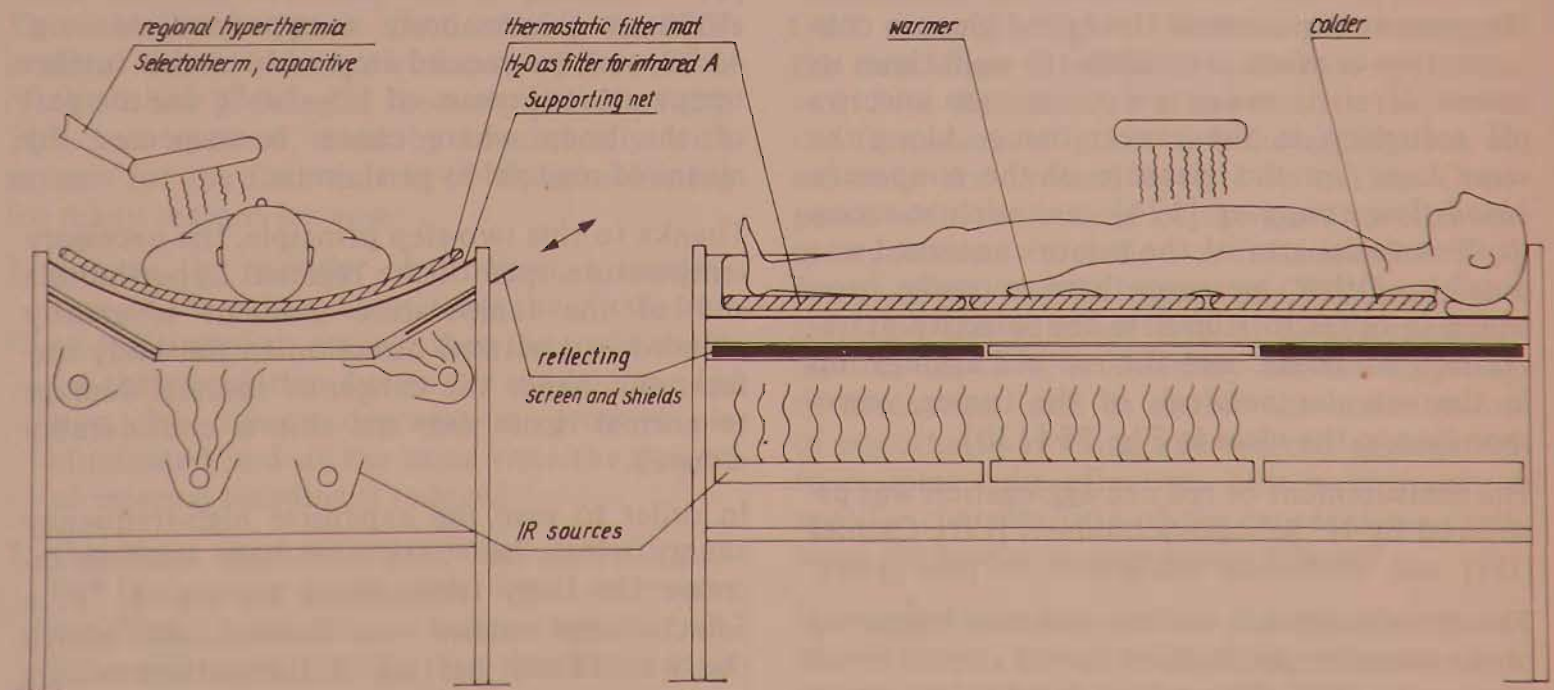


Fig. 77 Design of the selectotherm infrared equipment for two-step hyperthermia to generate tissue temperatures in different body sections. High temperature gradient in body through adaptable partial irradiation and cooling, and additive regional hyperthermia. Patient freely accessible for necessary manipulations (glucose infusion, O_2 -application, temperature measurement on several sites, surveillance. For the present state of technical realization, see Appendix.

forms with axial eddy current field it was possible to exclude the "body contour effect" (Fig. 80), and, as Fig. 81 shows, to increase the energy deposition, e.g. at a phantom depth of 5 cm, from 25 to 50 % [77, 142].

The comparison of photographs taken after an interval of 3 weeks (Fig. 82) proves that the combat of tumors can be clinically successful with the CMT concept using two-step hyperthermia by the Selectotherm method. At present

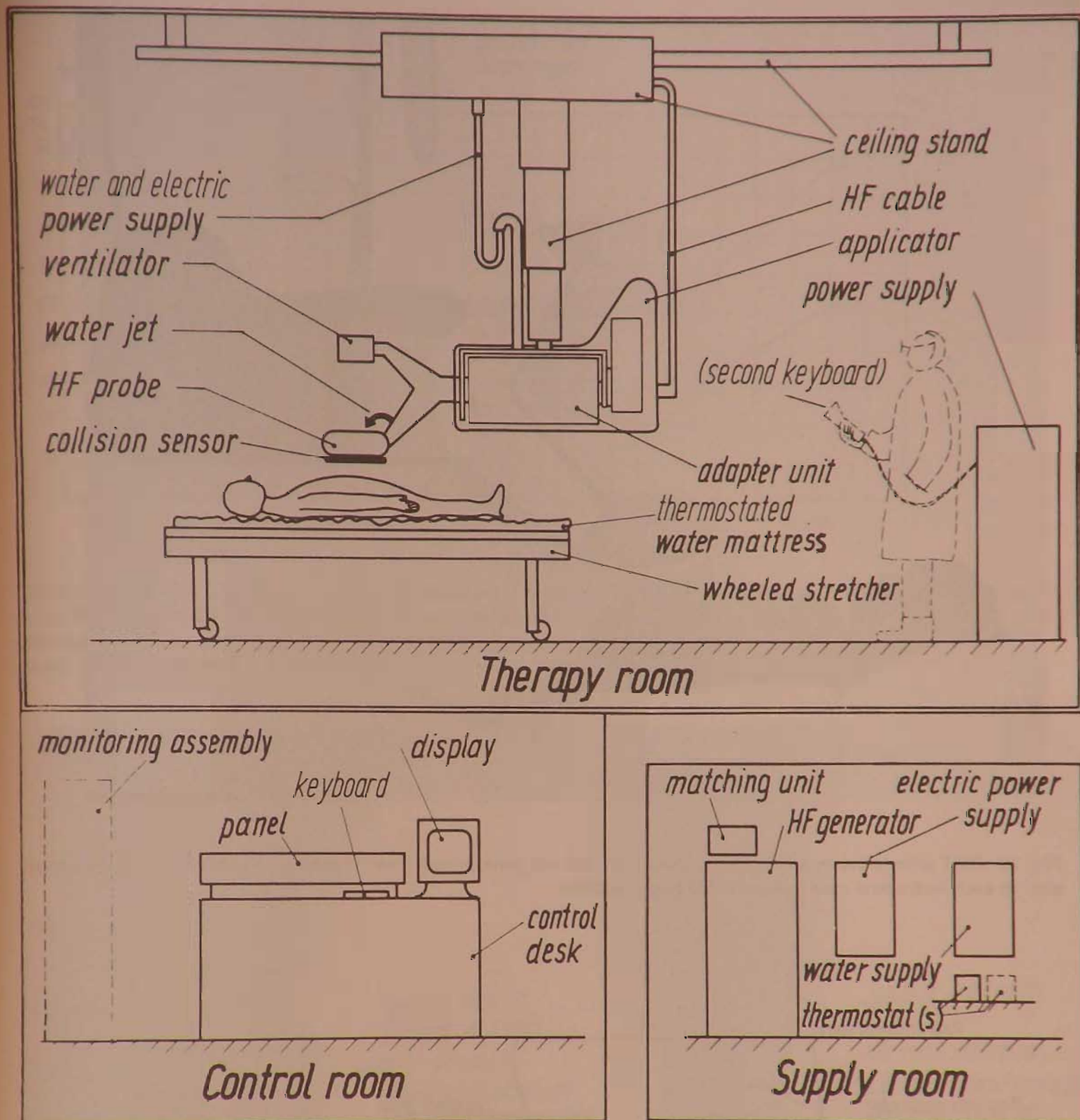


Fig. 78 Schematic presentation of the CMT selectotherm 111 equipment for homogenized energy deposition into the body's center (e.g. $T_N = 41.5^\circ\text{C}$) and into regions suspected of cancer ($T_C = 42.5^\circ\text{C}$). Two-step hyperthermia with O_2 inhalation

we are working to increase the probability of such results, in particular by means of favorable control of the selective hemostasis and the cellular capillary wall switching mechanism (cf. Fig. 75, intensification of vascular leakage and of red cell aggregation in the tumor region).

If the explanations in this paragraph seem too extensive, it should be remembered that the easily controllable and homogeneous regional hyperthermia of parts of the body, just like the

whole body hyperthermia, is also of great interest for other branches of medicine (diseases of the apparatus of locomotion, such as rheumatism, etc.), and that the simultaneous support for the circulation by means of the O_2MT procedure can extend the range of application, particularly in older patients. It should also be remembered that the mechanism of vascular obstruction, which is the target in CMT, is almost exactly the same mechanism which in myo-

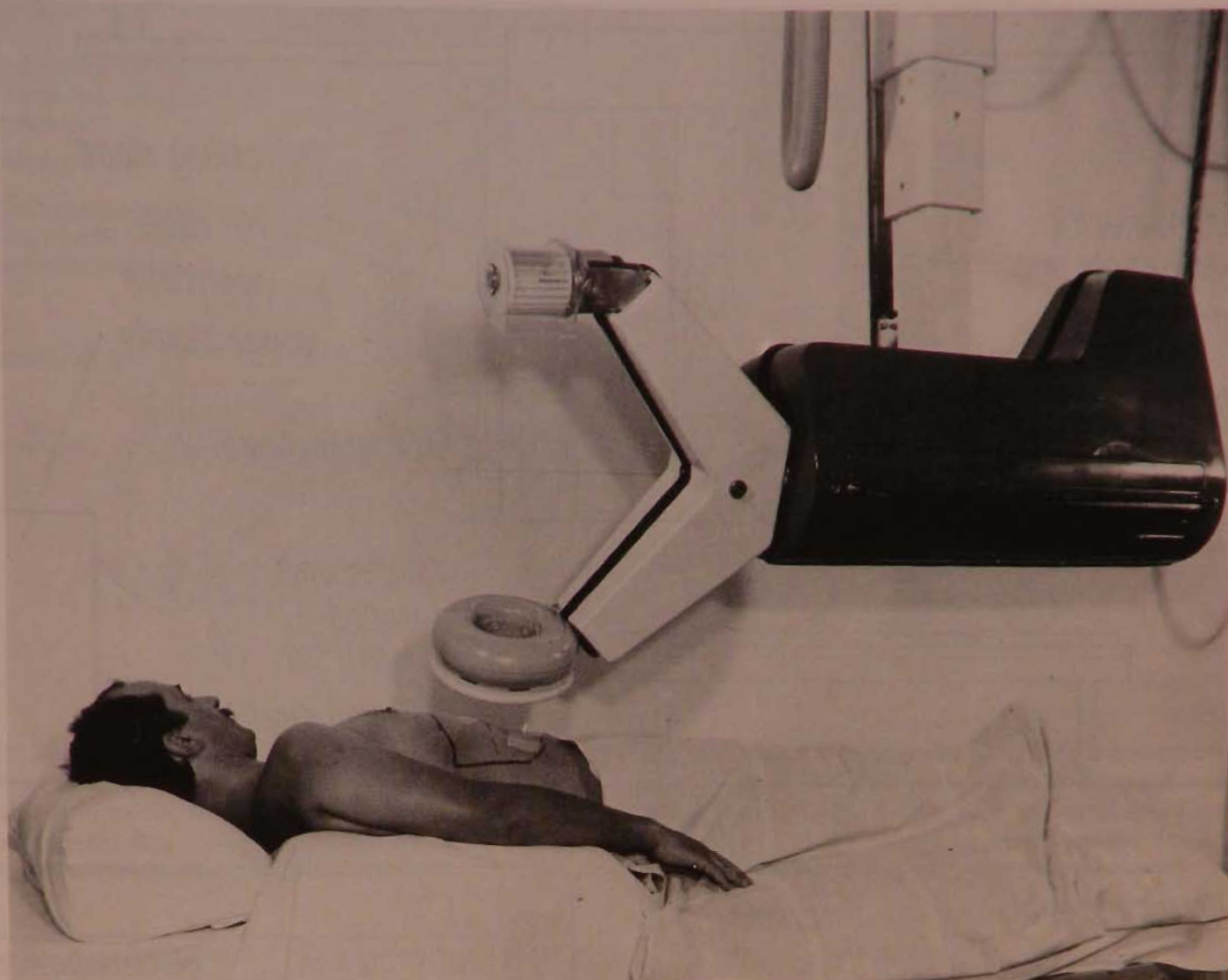


Fig. 79 CMT selectotherm applicator system (3rd and 4th generation). The rf heating coil moves on orbits adaptable to each individual case over selected body sections

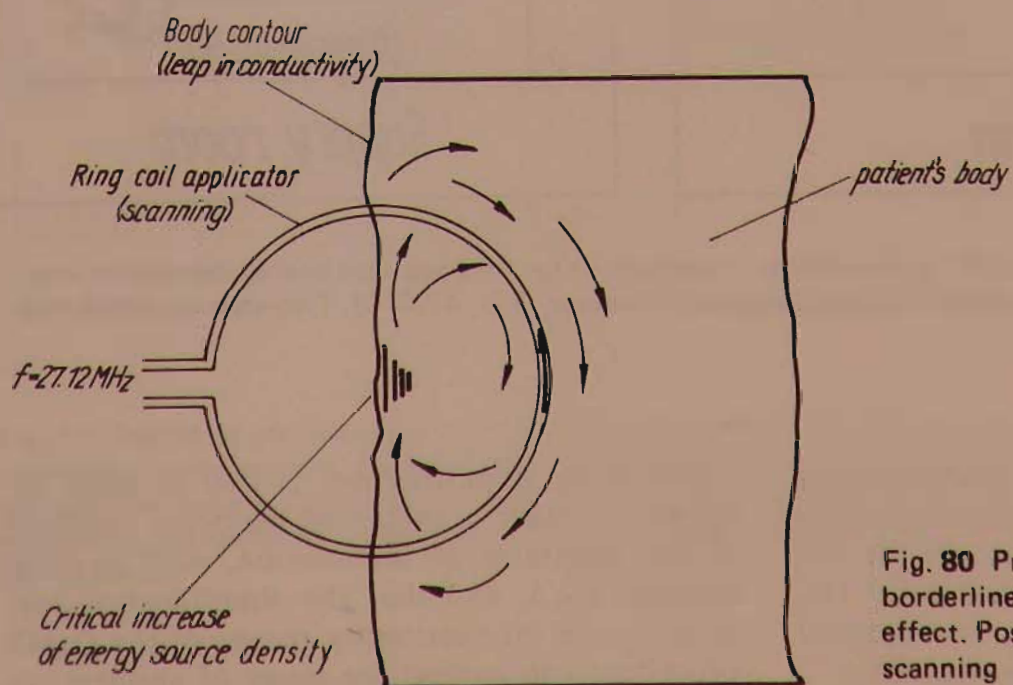


Fig. 80 Presentation of the over-heating of borderline tissue as a result of the body-contour effect. Possible momentary picture during scanning

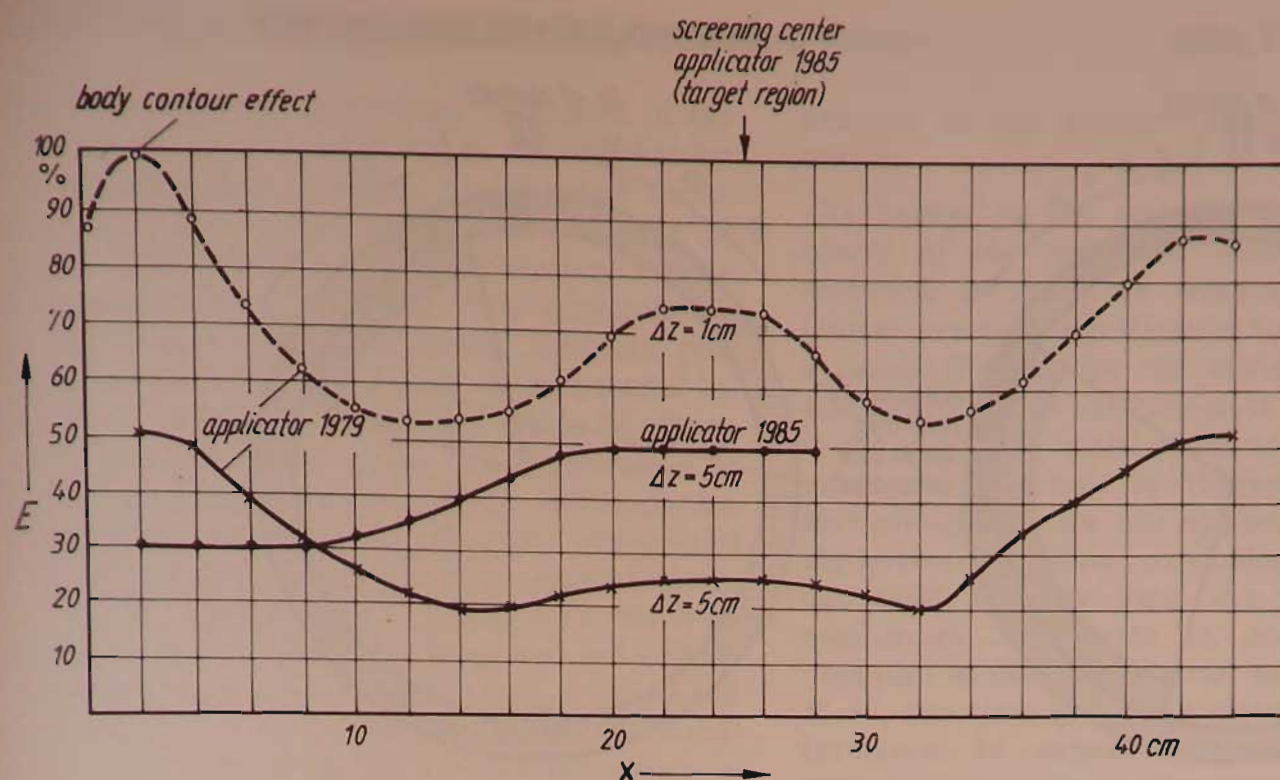
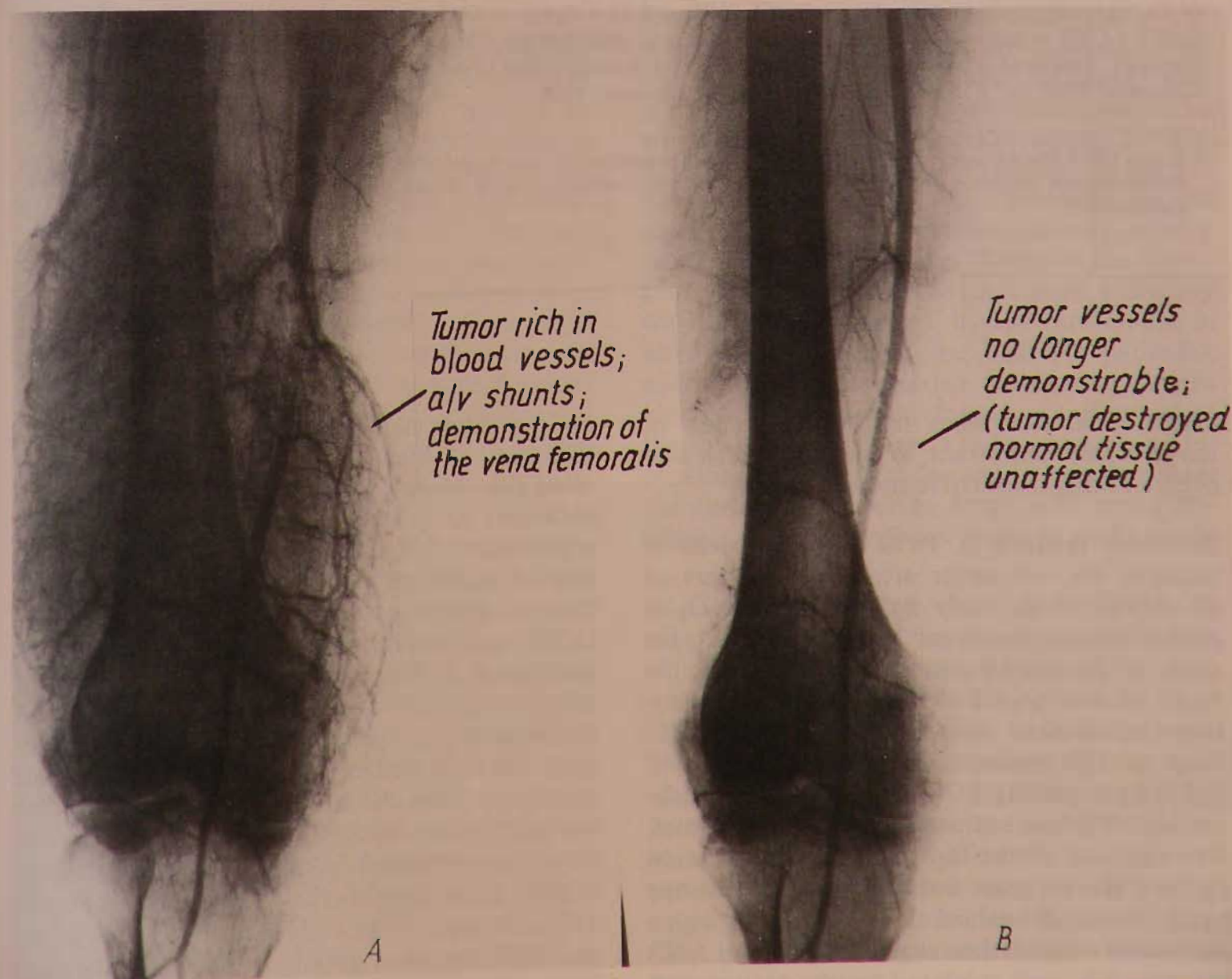


Fig. 81 Measurement of the relative energy deposition at various depths in an agar phantom with a ring coil applicator 1979 ($R = 8.25$ cm, distance $z_0 z_1 = 11$ cm, rectangular scanning with $x = \pm 16$ cm and $y = \pm 10$ cm) and with the new applicator 1985 (distance $z_0 z_1 = 11$ cm, circular scanning with $R_0 = 10$ cm). Advance: Increase in energy deposition at a depth of 5 cm from approximately 25 to 50%



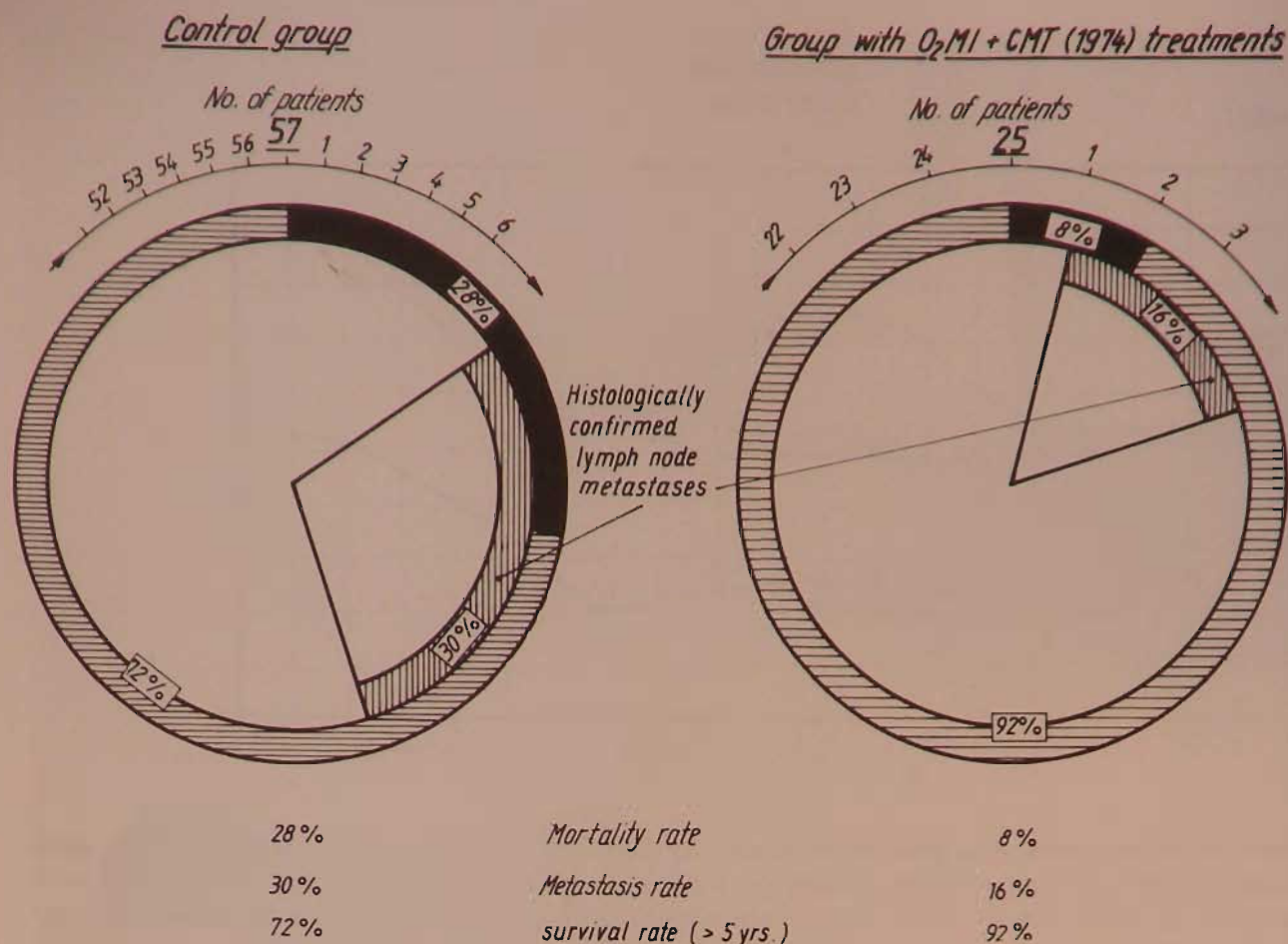


Fig. 83 Reduction in rate of metastasis in histologically proven cervical carcinomas (mainly stage IIb) by means of O₂ multistep immunostimulation O₂MT (BCG and 32 h O₂MT) + CMT (concept 1974)¹ from 30 to 16% O₂MT + CMT as adjuvant therapy to the conventional oncotherapy (OP according to Wertheim-Meigs, radiation therapy). Treatments between 1974 and 1978 at the Gynecological Clinic of the Medical Academy, Dresden (Director: Prof. Dr. B. Sarembe), M.D. thesis by C. Kaiser, 1985

¹ Since 1974 the efficacy of the concept has been significantly improved through methodological and technical development (thymus preparations, e.g. Neythymun instead of BCG, Selectotherm equipment of the 3rd generation)

cardial infarction leads to the destruction of tissue highly important to life, and which also occurs during irreversible shock.

Since we realized in 1970 that conditions of collapse do not occur after several hours of 40–41 °C whole body hyperthermia if O₂ is applied during the hyperthermic phase [2], the steps of the O₂MT and, from 1974 [143], the steps of the O₂MT immunostimulation have been included in the CMT program. The efficacy of this measure was increased in 1977 [125] by replacing BCG as an immunomodulator with thymus extracts, CEH or Neythymun. The addition of the O₂MT immunostimulation in the CMT program was successful, on the one hand, in that it enabled us to aim for as high a body core temperature as possible (e.g. 41.5 °C) for, e.g. 3 h, well tolerated by the patient and,

on the other hand, in the immunological destruction of the cancer cells which have survived the therapy. That is, we are striving for a *reduction of the probability of metastasis and recurrences*. Our ideas on the reduction of the rate of metastasis and the increase in the cure rate by means of the adjuvant procedure of O₂MT immunostimulation have been clinically confirmed, as Fig. 83 shows. The study carried out between 1974 and 1978 on patients with histologically proven cervical carcinoma (mostly stage IIb) showed a reduction in the rate of metastasis from 30 to 16% and a drop in the mortality rate from 28 to 8%. This result, which was obtained 5–6 years after treatment, carries great weight for the reason that the 1974 concept of the O₂MT immunostimulation and CMT has been greatly improved since then by methodological and technical developments.

1.2.3 Myocardial infarction and oxygen multistep therapy

As soon as a high percentage inhibition of the microcirculation occurs due to the mechanism of capillary/post-capillary blood vessel occlusion discussed (cf. Fig. 75), the drainage of lactic acid formed by fermentation is also hindered (hidden acidosis). This accumulation of lactic acid triggers a further feedback process, in the CMT procedure, in myocardial infarction and also in the late phase of shock with some temporal delay: the deceleration or stopping of the drainage of lactic acid leads to a gradual reduction in the pH at the venous and of the capillary from at first approximately 6.6 to 6.7 down to 6.0. Linked with this is an increase in the vascular leakage and red cell aggregation, and also a further loss in blood cell flexibility, i.e. an intensification of the occlusion. The time required for this pH reduction was determined at 150–200 min by in vivo pH recordings for CMT conditions. The time-span until steady-state overacidification is reached seems to be considerably shorter under infarction conditions (high-rate formation of acidic metabolites by the permanently working heart muscle).

This double feedback process explains the suddenness with which the infarction overcomes the victim. At the same time it can also be understood, however, that the infarction can be eliminated with the same suddenness in the initial phase of the acute ischemia, by a measure which increases the tissue pH. The portrayed *double feedback process in the triggering or interruption of the infarction* is a theoretically significant characteristic of the myocardial infarction which has hardly been discussed in cardiology as yet, perhaps because, although its pathogenetic rank in medicine was probable from observation, it is and can be seen in its functional context much more clearly by physiology and physics.

After the reduction of the pH in the myocardial tissue concerned, there follows in the course of some 10 min the cellular release of lysosomal enzymes, which are activated with a factor of virtually 10 at pH values of around 6, and instigate the destruction of the relevant cells [141]. As soon as the outer cell membrane has been destroyed after about 100 min, the lysosomal enzymes which then enter the extracellular space contribute to the damage of neighboring cells, and the *lysosomal cytolytic chain reaction of the myocardial infarction* [144], discussed below, proceeds after a further time delay of one to several hours, which in turn finally leads to the homogeneous large-area

necrosis in the affected region of the heart muscle.

The answer to the *question of how long the course of the infarction mechanism remains reversible in the given temporal course* is of crucial practical significance for the design of a causal therapy for the initial phase of the acute myocardial infarction. It is only possible in the reversible initial phase to bring the acute infarction to a halt by therapeutic measures. Measures which are not applied until later, in the irreversible phase, particularly in the clinic, can only spatially limit the self-maintaining mechanism, ameliorate it, and support the organism so that it can better survive, or survive at all, the time-span with reduced cardiac performance. In animal experiments we ascertained the amount of time up to the beginning of the irreversible tissue damage in the rat, by means of pH measurements in the rat heart, described below, under the conditions of a myocardial infarction triggered by a coronary ligature. We found that the transition from the reversible to the irreversible phases occurs approximately 20 min after the infarction is triggered. If we use as a basis our estimation that pharmacologically therapeutic measures, with the aim of interrupting the infarction in its reversible phase, must be taken within 20 min, then it necessarily follows that *only the patient himself can undertake this primarily helpful measure*, as medical treatment is only in very rare cases available within 20 min of the infarction. It follows from this that only a therapy which has been prepared by the cardiologist in attendance (especially for high-risk patients), and which can be carried out by the patient himself, can restrict the triggering and spread of the infarction mechanism in an acute case. This conclusion practically forces us to *restrict these therapeutic measures to drugs with a fast and reliable effect when given orally or perlingually*.

One drug which fulfils this task supremely, as long as certain limits are observed in its dosage and application, is *g-strophanthin*. This drug, which was popular as a cardiac glycoside about 50 years ago, has nowadays been pushed well into the background, particularly by the slow-acting digitalis preparations. This is strange, because the very fast occurrence of the *g-strophanthin* effect (approximately 6 min after administration, compared with 90 min for digitoxin [145]) means that the ranges of indications partially overlap each other. Above all, however, therapeutic effects have been proven

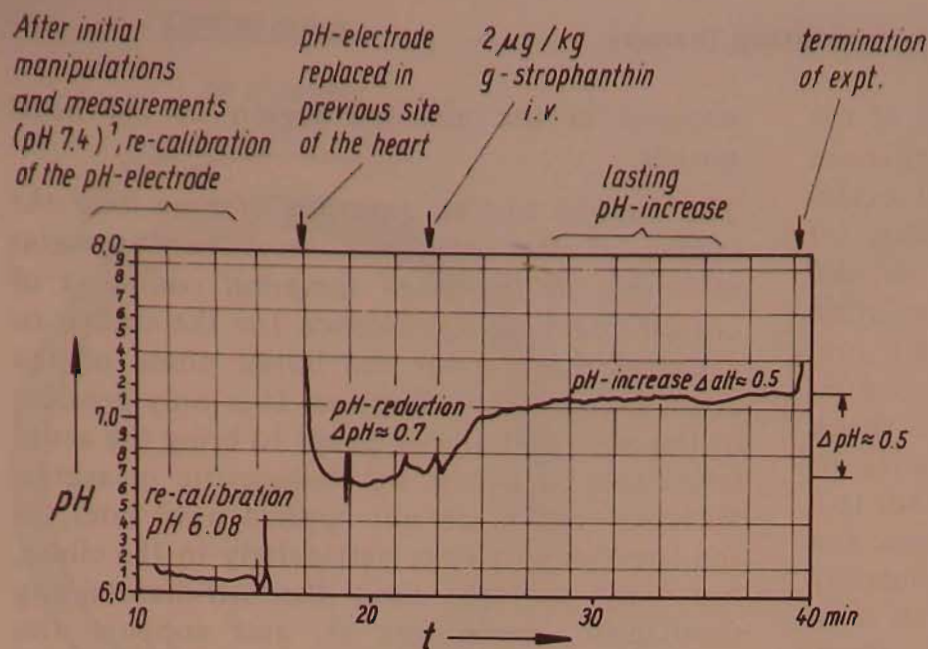


Fig. 84 The long-lasting, pH-increasing effect of g-strophanthin in the left ventricle of the myocardium [146]. pH changes during the early phase of an experimental cardiac infarction simulated by a controllable (clamping, lifting) ligature of a coronary vessel of the beating rat heart, and after i.v. injection of g-strophanthin. Part of an original strip-chart recording. pH measurements using a glass combination microelectrode

¹ Not shown here

for g-strophanthin, which have not been observed with digitoxin. Thus we found in accordance with Fig. 84 that the pH in the focus, which had fallen during an experimental infarction, rose again within 4 min of a dose of g-strophanthin [146]. The view, which can be found in old textbooks of cardiology, that g-strophanthin stimulates the degradation of formed lactic acid as an energy source of the heart muscle, can help us to interpret this. If g-strophanthin moderates in the initial phase the over-acidification which occurs in the focus, then the reversible formation of "pores" in the vessels and the stiffening of red cells and leucocytes must also be reduced, and the staunching of the microcirculation which has occurred must be more or less lifted. We have tested this conclusion with experiments. The confirmation of its correctness can be seen from the measurements summarized in Fig. 85. Photoelectronic measurements of the color index of the tissue with a micro-optical wave guide [121] did indeed show that the value in the focus greatly rises immediately after a dose of g-strophanthin (Fig. 85 A), that therefore the microcirculation is increased again [122], which leads to a favoring of lactate drainage and hence to a rise in pH. The mean oxygen partial pressure in the tissue was also simultaneously recorded in these experiments (Fig. 85 B). From this record it can be seen that, roughly at the same time as the increase in microcirculation caused by g-strophanthin, the mean P_{O_2} in the focus also increases considerably. It has thus been proven in animal experiments that g-strophanthin, applied early enough, can weaken the critical feedback process discussed, and restrict the infarction mechanism.

In attacks of angina pectoris, too, g-strophanthin causes, over and above the effect of the in-

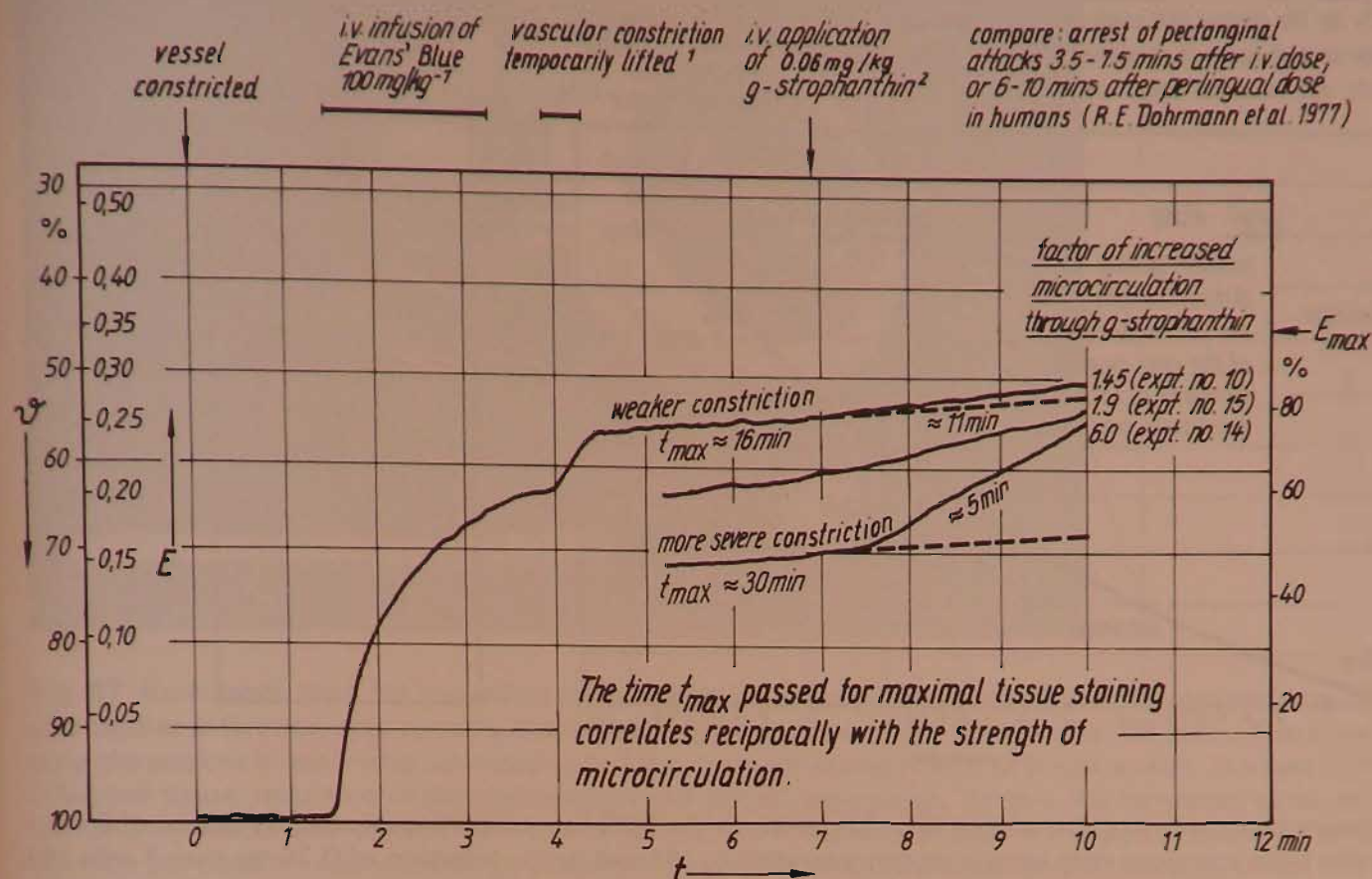
crease in pH, an increase in the microcirculation and thereby also in the O_2 supply in the area concerned. The result is, as a rule (in approximately 85 % of cases [147]), an arrest of the angina pectoris attacks within 6–10 min of an ad hoc application.

A renaissance in the use of g-strophanthin can be expected following these findings if we can refute a claim which, despite experimental counter-findings, is unfortunately brought forward again and again: the incorrect claim that g-strophanthin cannot even be given perlingually with certainty of effect¹.

It follows from our investigation [150], in accordance with Fig. 86, that the strength of action of the oral/perlingual dose is largely dependent on the concentration of the solution applied. This means that the strength of action depends significantly on the accidental dilution of the glycoside with saliva, i.e. that considerable variations in the effect can be expected with this type of application. These variations can be avoided, however, and a high effect on the heart achieved, equivalent to the i.v. standard dose, if the dose (according to [15]) is applied perlingually in high concentration (e.g. from a Strodival special preparation, 6 mg = 6 % in oleophilic phase). The administration is

¹ The idea that perlingually applied g-strophanthin is only slightly resorbed, and at a high degree of variation (Greeff, Verspohl) must be held to be incorrect, since it was shown in [148] that the applied g-strophanthin is found at its maximum concentration in the plasma only 24–48 h afterwards, and Erdle confirmed this result in his thesis [149]. According to [148], in this proportion of g-strophanthin released from the (tongue) tissue, we are only dealing with a residual molecule which is hardly toxic any more, and without glycoside effect

A Measurement of the dye inflow E in the circulation area of a narrowed coronary vessel



B Measurement of the mean pO_2 in the circulation area of a narrowed coronary vessel

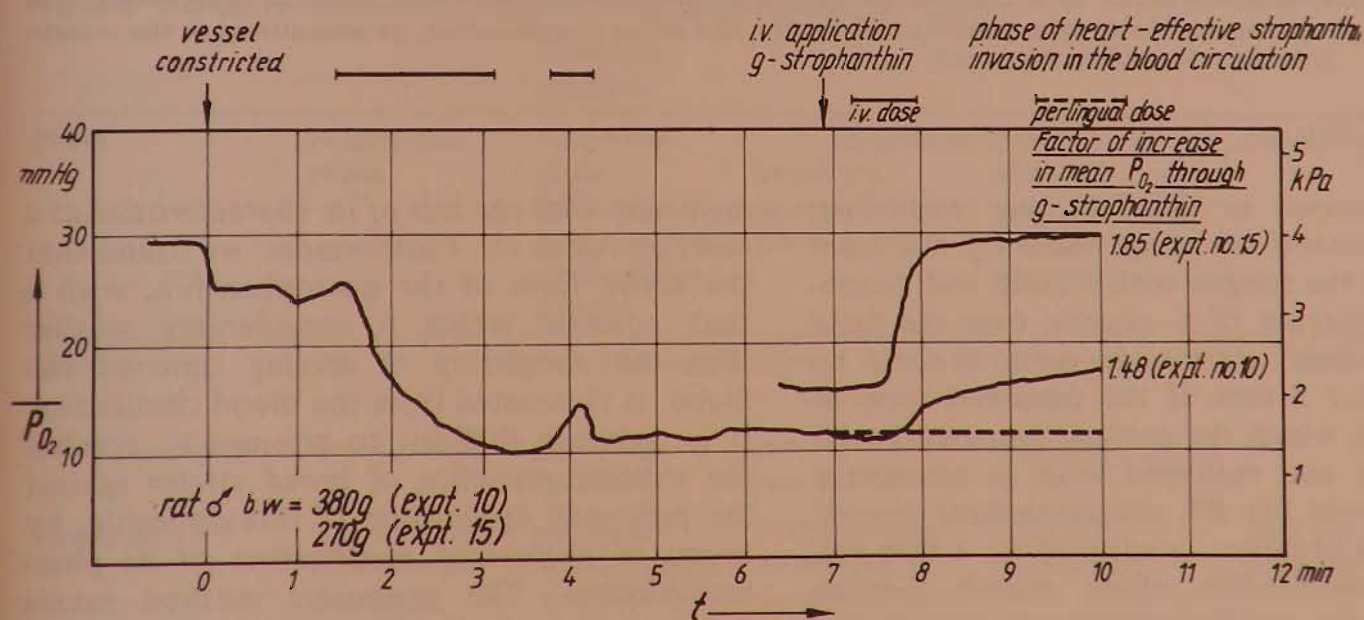


Fig. 85 Direct proof of restoration of microcirculation (A) and in the mean P_{O_2} (B) in the circulation area of a coronary vessel constricted to simulate cardiac infarction, immediately after application of g-strophanthin. Vital colorimetric measurement (A) using light-conducting micro-probe. Needle of light probe ground flat and attached on the tissue area of interest. ϕ = transparency, E = extinction

¹ Experimental control

² Dosage adapted to species rat

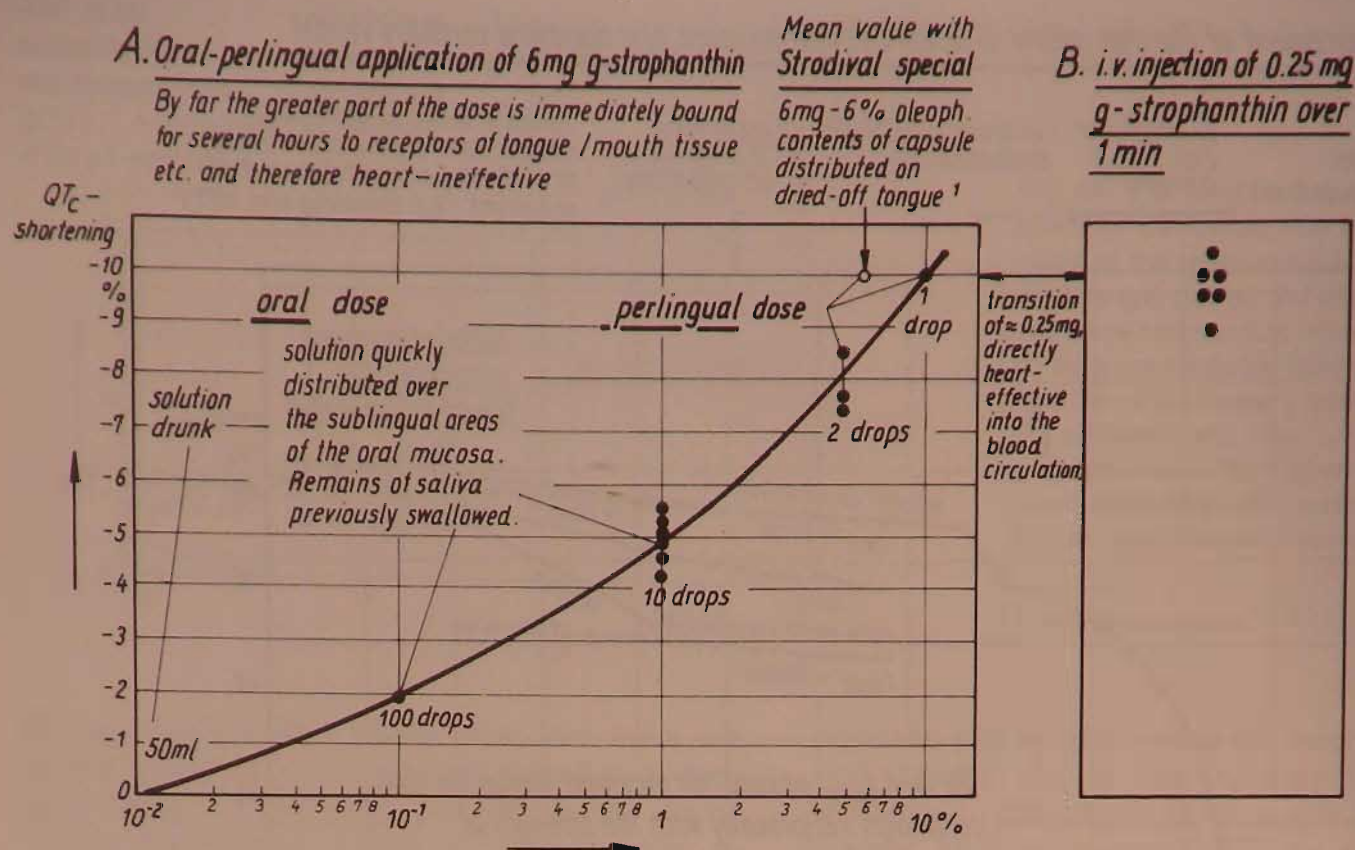


Fig. 86 Measurements showing the relative QT_c shortening in the ECG by oral-perlingual administration of 6 mg g-strophanthin from solutions with increasing concentration c_s (A) and by i.v. injection of 0.25 mg over 1 min (B). Result: The effect of the i.v. standard dose is only equivalent to the safely applicable 6 mg perlingual dose ($\geq 6\%$ in oleophilic phase) with due consideration of the mode of application described

¹ First swallow remaining saliva. After distribution, rapid shallow respiration for 3 min. Onset of heart effect (also QT_c shortening) approx. 6 min after administration. With this mode of application, no side-effects in the intestinal tract

to be practised in the following way: first, swallow remains of saliva, then dry the front surface of the tongue with a cloth and distribute the contents of a capsule over the dried tongue surface; afterwards rapid shallow respiration for 3 min. If the described form of application, which the patient, prepared by his cardiologist and equipped with an emergency package as in Fig. 87, can implement himself in an acute situation, is adhered to, a *high and reliable strophanthin effect occurs*. Grabka [151] reports on the significant drop in the mortality rate of infarction after the introduction of immediate therapy with g-strophanthin (Strodival) given perlingually, in underground mining.

Unfortunately, the pharmacokinetics of this drug given i.v. and perlingually are very unusual and complicated [148]. This behavior is a consequence of the fact that this glycoside is bound within fractions of a second by the receptors of the outer cell membranes (also of the tongue tissue in particular), and is *not dissociated from the receptors until 2–4 h later, and then only with slight modification of its*

molecule, with the loss of its characteristics as a heart glycoside (!). Furthermore, we found that the active form of the g-strophanthin, with a time constant which is considerably smaller than the circulation or mixing time of the blood, is eliminated from the blood circulation. It is therefore difficult to attempt to combat the existing prejudice of broad circles against the perlingual application of this glycoside, by means of theoretical clarification of its pharmacokinetics. The pragmatic method seems to be more convincing here.

The therapeutic chance is much smaller if the counter-measures, as is normally the case today, are not undertaken by the clinic doctor until 15–20 min after the onset of the infarction, i.e. not until the infarction mechanism has assumed an irreversible character. It could be seen from measurements of the microcirculation with the dye-injection method, that even after the progression of the mechanism described and transition to the irreversible phase, a *proportion of microcirculation of some per cent* still remains until the onset of the lysosomal cytolytic chain reaction. Thus there exists for



Fig. 87 Emergency pack for immediate perlingual self-application of g-strophanthin for risk patients. The process of a cardiac infarction only remains reversible for up to approximately 20 min after its onset. Therefore it is usually only the patient himself who can make use of the often life-saving effects of strophanthin: increase in the pH in the infarcted tissue, reduction of plasma evasation and red cell aggregation. By this, the hampered blood microcirculation and O_2 supply are restored. Safe and reliable action by definite dosage of 6 mg g-strophanthin as 6% oleophilic solution per capsule, administered by distributing over the previously dried tongue. Onset of effect $\approx$ 6 min after application

Table 8 The various treatment phases in combatting a myocardiac infarct.

Phase	Prophylaxis phase	Emergency situation	Admission to clinical treatment		
		Reversible phase still a high level of therapeutic responsiveness	Irreversible phase before the cytolytic chain reaction occurs	after the cytolytic chain reaction has occurred	Rehabilitation phase
Duration	< 0	0 to 20 min	20 to $\approx$ 120 min	$\approx$ 120 min to $\approx$ 2 days	> 2 days
Microcirculation	almost normal	still almost normal	sinking to as low as 1%	sunk to as low as 1%	—
Measures	O_2 multistep regeneration procedure Strodival special Nitrangin	perlingual self-application of 6 mg = 6% g-strophanthin	Administration of the lysosomal stabilizer methylprednisolone, combination process O_2 MT + HOT* standard measures	Standard measures	36 h O_2 multistep procedure
Effect	Alleviation of angina pectoris and arrhythmias Increase in output	often a total stop of the infarct after 6 to 10 min	Extension of the lysosomal cytolytic chain reaction prevented	Combatting of the further progression of the large-area infarct necrosis	Increased physical performance Reduced patient risk

↑
onset of
myocardiac infarct

roughly 2 h the justified prospect of favorably influencing the further course of the infarction by suitable measures. In 1971 we suggested for this [144] that the *dose of g-strophanthin be supplemented by a lysosome stabilizer (e.g. methylprednisolone) in order to hamper cytolysis and cytolytic chain reaction*. By means of the treatment of 270 infarct patients with the suggested combination, Dohrmann achieved a drop in the mortality rate from 38 to 16% [152, 153] in his unselected patient sample in the Evangelisches Waldkrankenhaus Spandau, Berlin (West). After these particular reports, it is enough for the further therapeutic action in this critical time-span of such practical importance, to refer to the comprehensive, more recent literature on clinical infarction therapy [154]. The experiences gathered in the last few years entitle us to estimate that the wide use of the discussed results of Dohrmann's and our groups could lead to a drastic drop in infarct lethality. The way to this is to abandon [155] the old-fashioned pharmacological ideas on the lacking efficacy of the perlingually administered g-strophanthin.

Strophanthin is also of significance for other medical disciplines, in addition to its use in myocardial infarction, particularly in situations where there is lactic acidosis, e.g. in sports medicine. According to as yet unpublished self-experiments by my co-worker W. Klemm, sporting performance capacity is increased in the anaerobic boundary region (with lactate accumulation). The same performance could be achieved on a bicycle ergometer at a lower heart frequency after perlingual administration of one Strodival capsule.

From the above consideration we can recognize *several treatment phases of the acute myocardial infarction with differences regarding suitable measures, effects and the chances of success*. Table 8 gives an overview of these.

The consequences of the O_2 deficiency in a large volume of muscle tissue have been particularly thoroughly investigated in myocardial infarction. Thus Fig. 88 can give an idea of the *joint destruction of finer blood vessels in a large-focal necrosis in the final stage of the infarction* [156]. A comparison of this figure with the X-ray arteriography, Fig. 82, is very informative and shows that a mechanism very close to nature is triggered in the cancer tissue with the modern CMT concept.

O_2 inhalation is one of the standard measures in the therapy of acute infarct. An improvement in the O_2 status, as fast and as strong as possible is thereby strived for. Our PO_2 meas-

urements lead us to believe that progress could perhaps be achieved if, as described in the following paragraph, a HOT* procedure were implemented *simultaneously* with the O_2 application and a further raising of the η -value and the blood fluidity were thereby also achieved even under unfavorable circulatory conditions.

It also seemed necessary to go into detail in the discussion of the complex process in the triggering, course and therapy of the acute myocardial infarction, because we are dealing here with one of the main causes of death of our time and because a great change is occurring at present in ideas about the mechanism involved and the suitable counter-measures.

With the meaningful use of variants of the O_2 MT it should be possible greatly to reduce the probability of suffering a myocardial infarction. A *prophylaxis of a myocardial infarction* which attacks the primary cause exists when it is possible decisively to reduce the probability of O_2 deficiency in the heart muscle, lasting for some minutes, which triggers the infarction [111, 157]. One of the most effective means of avoiding such O_2 deficiency conditions is the use of O_2 MT and (or) exercise training in order to raise the O_2 status which has been critically worsened in increasing age or due to distress.

In the *rehabilitation phase following myocardial infarction* it seems possible to *reduce considerably the risk of reinfarctions* and to shorten the period of recuperation, e.g. by application of the 36 h O_2 MT procedure, GK 4-I. The patient's stress capacity increases considerably even during this procedure, in correlation to the rise in the PO_{2-art} measured without additional O_2 application, or in the η -value. This fast increase in the strain capacity is of specific significance for rehabilitation after a myocardial infarction; until now treatment here has had to tread a tightrope between triggering a recurrent infarction due to too much strain, and an unnecessarily slow return to a suitable way of life in the case in question, due to too little strain. This tightrope is broadened and the risk to the patient thereby significantly reduced by means of the discovered "initial mobilization" of the infarct patient, which, in the example in Fig. 89, occurs after the first sessions of the 36 h O_2 MT procedure. Thus the mobilization effect of the O_2 MT signifies a decisive aid to rehabilitation after myocardial infarction, which should be taken up with as little delay as possible by all medicinal branches concerned with this problem. In order that this demand can be more easily understood and accepted, we will report here the observations made in a single,

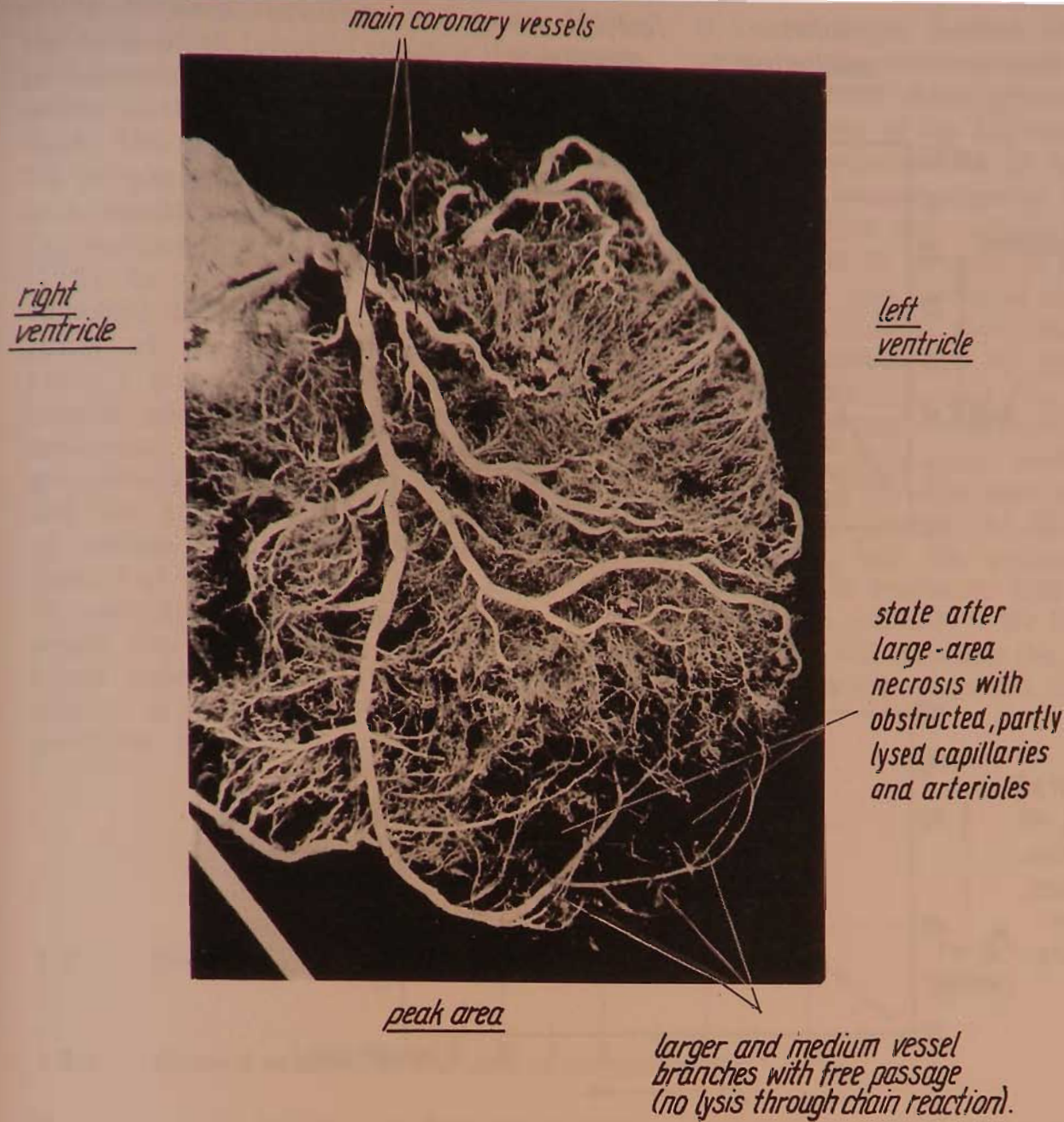


Fig. 88 Large-area necrosis and damage to blood capillaries. Postmortem coronarography of a myocardial infarct in the peak area of the left ventricle, according to Baroldi. In the volume of the large-area necrosis the capillaries and finer arterioles are occluded, and partially lysed. The functional elimination of the finest vessels is the final consequence of a longer-lasting deficit in O_2 utilization in a greater volume of tissue

characteristic case. A middle-aged patient comes to us in Dresden soon after a myocardial infarction, in order to undergo O_2MT . On the day of his arrival his PO_{2-art} is low, and he can only climb to the second floor of his 13-storey hotel, as severe anginal complaints prevent him from climbing further. After just three sessions, each of 4 h, this movement disability disappears, and the patient climbs all 13 storeys of his hotel without any anginal complaints (no signs of decompensation). Due to the "initial mobilization" he is now able to undertake

regularly the obligatory exercise training of our 36 h O_2MT procedure between the sessions. At the end of the cure, and even weeks afterwards, an increase in his PO_{2-art} of around 20 mmHg is measured. Afterwards the patient repeats his climb to the 13th storey of his hotel twice more without complaints. The described effect of the O_2MT procedure on the lung-heart system is not only of significance for rehabilitation after myocardial infarction, but should be used generally for rehabilitation after illnesses, operations, accidents and other health crises.

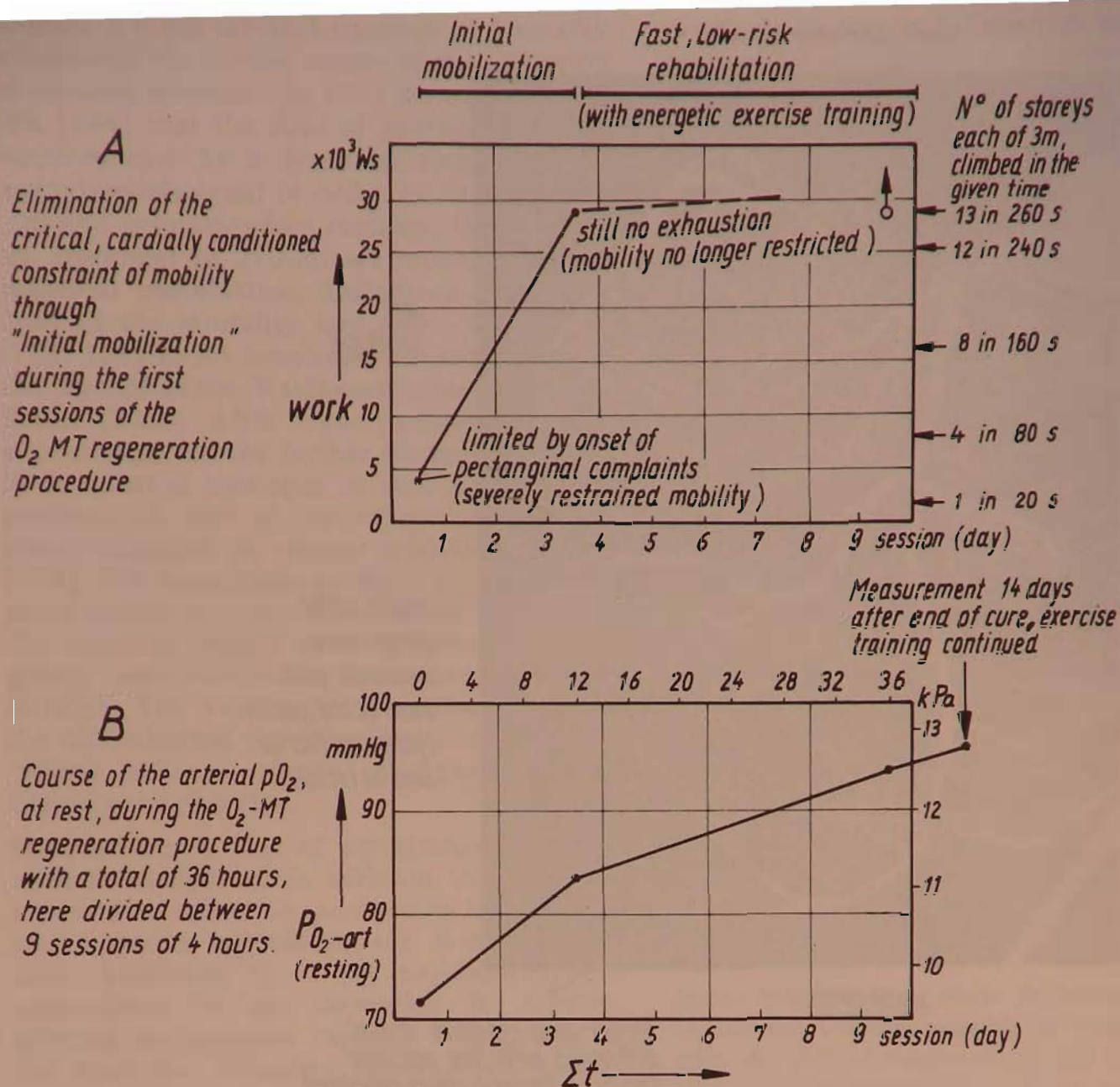


Fig. 89 Example of risk reduction and speeding-up of rehabilitation in a 55-yr-old infarct patient through initial elimination of cardially-conditioned constraint of mobility with the aid of the O_2 MT procedure GK 4-I (A). This "initial mobilization" of the patient is of principal importance for the general problem of rehabilitation and is closely connected with the increase in the arterial resting pO_2 (B) and the decrease in the venous resting pO_2 occurring during the O_2 MT cure (increase of physical fitness)

1.2.4 Shock syndrome and oxygen multistep therapy

Shock is a clinical syndrome affecting ill persons with more or less acute onset of circulatory insufficiency; ill persons who are peculiarly dazed, sense increasing weakness, whose extremities are cold, and whose skin is cool and damp, who have a fast, weak pulse, in whom the excretion of urine decreases more and more, and in whom a drop in the arterial blood pressure can frequently – but not always – be measured. If the various causes which attack the different sites of the circulatory system are not eliminated in time – in other words, if the "point of no return" has been reached – than the causes and consequences of the acute circulatory insufficiency superimpose: the

shock becomes irreversible. Shock needs time for its development and its clinical picture is determined by the juxtaposition of cause, host's compensation mechanism, and general and local consequences, which sometimes form a vicious circle. The purpose of the circulation is fulfilled in its periphery, that is, in the direct neighborhood of the respiring cells and tissues. In this respect, shock is a more or less acute failure of the circulation, in which locally and pronouncedly the capillary circulation drops acutely to below the requirements of the tissues, simultaneously in several organs. Thus the microcirculation becomes the key to the qualitatively and quantitatively controlled inter-

the basis of all forms of shock is the common pathophysiological characteristic of the deceleration of the blood flow in the capillary network. The generally insufficient circulation in the periphery should be particularly considered here, especially the form which is triggered by O_2 deficiency from the most varied cause [158]. As with the selective vascular occlusion envisaged during the CMT, or with the mechanism of myocardial infarction, there also exists a reversible and, subsequently, an irreversible phase in the largely analogous shock syndrome. We believe that it is not only the precapillary sphincters (hindrance of influx) and the postcapillary constriction (hindrance of outflow) [158], but also the bioenergetic control of the cellular capillary wall regulating or switching mechanism, discussed above, which play a role in the slowing down of the blood flow in shock. The therapeutic intervention in shock can only be successful in the reversible phase. The counter-measure which

is consequently derived from the triggering cause is the *renormalization*, as fast as possible, or, even more effective, the *substantial improvement of the O_2 status in the reactive capillary endothelium*. In the usual treatment of shock events triggered by O_2 deficiency (hemodilution [47, 154]), the application of O_2 , as early as possible, is a matter of course. The speed and extent of the improvement in O_2 status brought about by this measure can be easily determined by the measurement of the resting PO_{2-art} and PO_{2-ven} values. Due to the circulatory insufficiency, the lowered PO_{2-art} is often only moderately raised. It should be a principle that the facilities should always exist further to increase significantly the PO_{2-art} and the η -value by means of a combination procedure with simultaneous O_2 application and HOT*. We hope that the above comments will stimulate the implementation of pilot treatments with this combination procedure.

1.3 Oxygen supply to the tissue

1.3.1 General remarks on the limit of oxygen supply

The oxygen reaches the cells from the capillary blood by diffusion and is used by them in oxidative metabolism, whilst the carbon dioxide released as an end-product is simultaneously delivered to the capillary blood. The drop in PO_2 , or increase in PCO_2 , which thereby arises between the arterial and venous ends of the capillary, has already been indicated in Fig. 9. Since O_2 deficiency in the tissue limits the oxidative cell metabolism much sooner than insufficient CO_2 removal does, it is enough here to consider only the O_2 supply to the tissue.

The limits of O_2 supply (diffusion distance) which surround the capillaries at distances of some 10 μm , represent the *start of the zone of*

cell decay in the living organism. They are of vital significance in the formation of the steady state between cell proliferation and cell decay in the intercapillary space of the tissue (organs). If these limits come too close to the capillaries, due to O_2 deficiency over a long period of time, then the cell decline triggered by this leads to a critical decrease in organ performances: *O_2 deficiency conditions or O_2 deficiency diseases* [159] occur. In special cases it is possible significantly to increase the O_2 supply by means of hemodilution or HOT* (improvement of the flow properties [47, 160]). The furthering of the O_2 supply limits is one task and an elementary process of the O_2 MT.

1.3.2 Vascularization parameters and the O_2 metabolism characteristic as the boundary conditions for the O_2 diffusion field in the intercapillary space of the tissue

The basis of most of the pathological consequences of O_2 deficiency in the human organism is primarily the principles of the O_2 supply in the intercapillary space of the tissue. These principles can be theoretically and quantita-

tively formulated for idealized models with relative little mathematical-physical effort, provided the boundary conditions are known [161–163], and they are easily comprehensible.

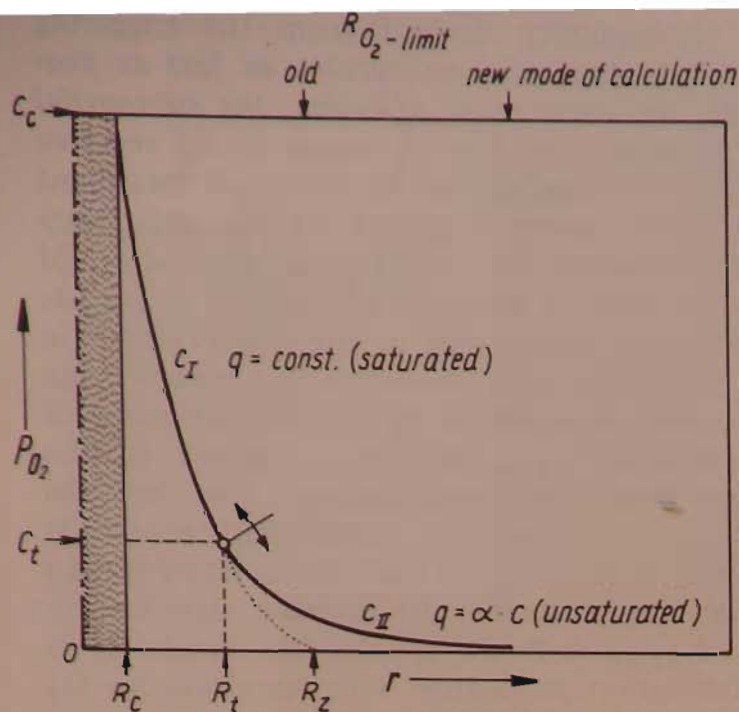


Fig. 90 Model of a single capillary with coaxial O_2 diffusion field. Symbols as for the solution of the diffusion field equation, see Table 10

r = radius, measured from the capillary axis
 c = concentration, i.e. O_2 partial pressure
 D = diffusion coefficient
 q = consumption of permeated substrate
 α = consumption constant = $\Delta q / \Delta c_{II}$
 R_c = capillary radius
 C_c = mean concentration in the capillary
 R_t = radius
 C_t = concentration
 R_z = fictitious supply area, Krogh's cylinder

$$H_{Ot}^{(1)} = H_o^{(1)} \sqrt{\frac{\alpha}{D}} R_t = \text{Hankel's function at the point } (R_t, C_t)$$

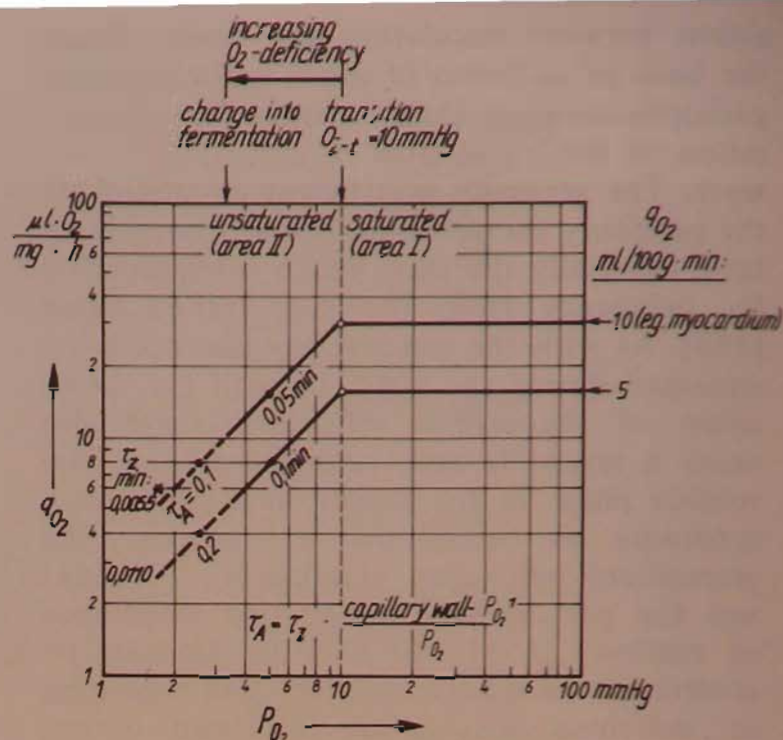


Fig. 91 Characteristic curve of the function $q_{O_2} = f(P_{O_2})$, i.e. oxygen consumption in dependence of the oxygen partial pressure in tissue. Idealized extrapolation according to data given in [164]. Parameters: P_{O_2} at the capillary wall, 45 mmHg; τ_z^* = time constant to the O_2 -consumption in tissue¹; τ_A = time constant of the O_2 -exchange circulation/tissue¹; q_{O_2} is defined as $\mu l O_2$ consumed per mg dry weight of tissue and hour

¹ For the definition of these parameters, see [2, 163]

Table 9 Mean values for the O_2 consumption, the blood flow rate and the arteriovenous difference in the O_2 concentration in the blood of various human organs at 37 °C [32]

Organ tissue		O_2 consumption q_{O_2} ml/100 g/min	Blood flow rate BF ml/100 g/min	a/v difference vol.-%
1 Myocardium	at rest	8 to 10	80 to 90	10 to 15
	under severe physical strain	to 30	300 to 400	to 17
2 Kidney	cortex	9 to 10	400 to 500	2.0 to 2.5
	outer marrow	6 to 6.5	120	5
	inner marrow	0.3 to 0.5	25	1 to 2
	total	5.5 to 6.5	400	1.5 to 2.5
3 Brain	cortex	8 to 10	80 to 110	10
	marrow	1	15 to 25	4 to 6
	total	3.5	50 to 60	6 to 7
4 Liver	total	4.5	60 to 100	3 to 3.5
5 Spleen	total	0.6 to 0.8	100 to 130	0.5 to 0.8
6 Skeletal muscle	at rest	0.25 to 0.5	2 to 4	10 to 15
	working hard	to 10	to 50	
7				
8 Blood		0.008 to 0.01		

For reasons of clarity we will consider here the simple model with a single capillary with a radius R_c and its O_2 diffusion field in the interstitium, as in Fig. 90.

For the calculation of the O_2 diffusion field of a capillary with a known radius and a known mean P_{O_2} of the blood flowing in it, it is necessary to know the size of the diffusion coefficient D for O_2 in the interstitium; also the volume of O_2 consumption q_{O_2} in the saturated range of the O_2 metabolism and the re-

duction in q_{O_2} in the unsaturated range. The O_2 metabolism characteristic of the tissue or cells gives numerical values for this. Its course for tissue or cells with an O_2 consumption $q_{O_2} = 10$ and $5 \text{ ml}/100 \text{ g} \cdot \text{min}$ (e.g. myocardial cells, liver cells) is given in an idealized form and rough approximation in Fig. 91. Mean levels of O_2 consumption in various human organs are given in Table 9, in accordance with [32]; this table also gives data on the mean rate of blood flow (BF) (indication as to mean vascularization).

1.3.3 Solution of the diffusion field equation of the O_2 concentration (P_{O_2}) in the intercapillary space, under consideration of the drop in O_2 consumption in the area of unsaturated O_2 metabolism

In the calculation of the concentration field of O_2 in the intercapillary space of the myocardium, we work from the diffusion of the substrate from a central capillary to the surrounding cylindrical tissue area, in the discussed simplified model. In all older papers on such a model [161, 162] it is assumed on the basis of approximation that the substrate consumption

in the tissue cylinder has a constant rate q (Table 10, area I). However, as soon as the metabolism is not loaded to capacity, the consumption q drops at the same rate, in accordance with the offer (area II). Guiding values for the transitional value $P_{O_{2-t}}$ have already been given in Fig. 91 (and Table 9, O_2 consumption). The hitherto simplifying type of calcula-

Table 10 The solution of the diffusion field equation for the oxygen concentration in the intercapillary space, taking into account the decreased O_2 consumption in the unsaturated area of O_2 metabolism in cancer cells

General diffusion equation:

$$\dot{c} = D\Delta c - q$$

at steady state conditions $\dot{c} = 0$

Vessel geometry assumed as cylindrically symmetric

$$\frac{d^2c}{dr^2} + \frac{1}{r} \frac{dc}{dr} - \frac{q}{D} = 0$$

$$\left\{ \begin{array}{l} c > c_t \longrightarrow q = \text{const.} \\ c < c_t \longrightarrow q = \alpha \cdot c \end{array} \right.$$

Area I: $c > c_t \longrightarrow q = \text{const.}$ (saturated)

$$c_I''(r) + \frac{1}{r} c_I'(r) - \frac{q}{D} = 0$$

Bernoulli's differential equation

BC:

$$\left. \begin{array}{l} c_I = c_k \\ r = R_K \\ c_I = 0 \\ r = R_Z \end{array} \right\}$$

Solution:

$$c_I(r) = c_k + \frac{q}{4D} (r^2 - R_K^2) - \frac{q}{2D} R_Z^2 \ln \frac{r}{R_K} \quad 1$$

Area II: $c < c_t \longrightarrow q = \alpha \cdot c_{II}$ (unsaturated)

$$c_{II}''(r) + \frac{1}{r} c_{II}'(r) - \frac{\alpha}{D} c_{II}(r) = 0$$

Bessel's differential equation

BC:

$$\left. \begin{array}{l} c_{II} = c_t \\ r = R_t \end{array} \right\}$$

2nd boundary condition (BC) neglected due to adaptation of the solution to the problem in hand

Solution:

$$c_{II}(r) = \frac{c_t}{iH_{0t}^{(1)}} \cdot iH_0^{(1)} \left(i\sqrt{\frac{\alpha}{D}} r \right)$$

Hankel's function, type 1²

¹ See [165, 166]

² For calculation of $H_0^{(1)}$ see tables of higher functions

tion of the cylindrical area supplied by the capillary, which only gives a rough approximation, can be seen on the left of Table 10. When the dependence of the consumption rate on the offer is considered, this area is very significantly extended. The solution of the diffusion field equation for the substrate concentration in the unsaturated area is presented in detail on the right of Table 10. The symbols are summarized in Fig. 90. The diffusion field equation presented satisfies our premises, whereby the consumption in area I is assumed to be constant,

and in area II to be linearly dependent on the concentration. The consideration of the stationary case simplifies the problem, so in area I a Bernoulli differential equation was obtained and in area II a Bessel differential equation. The boundary conditions which lead to the solution in both areas are also given in Table 10. The *two-dimensional diffusion field equation* is relevant for the PO_2 topography in supply of the vessel walls from the lumen, given and analysed in Fig. 243.

1.3.4 Selection of the equation parameters for oxygen and normally or deficiently supplied tissue

a) The oxygen partial pressure at the capillary wall in normal supply lies between 50 (venous end) and 90 mmHg (arterial end). In normal supply $PO_2 = 45$ mmHg (6 kPa) can be seen as a representative level for the middle of the capillary, and $PO_2 = 30$ mmHg (4 kPa) in deficient supply.

For a more accurate consideration of the effects of an increase in the PO_2 of the inhalation air, as envisaged by the second main step of the O_2 MT, it must be remembered that the drop in PO_2 occurs predominantly in roughly 25% of the capillary length, calculated from the arterial end [166], cf. also Fig. 3.

b) For the oxygen partial pressure in the transition zone from saturated to unsaturated O_2 metabolism of cells, $PO_{2-t} = 10$ mmHg must be used, in accordance with the characteristic in Fig. 91.

c) For the diffusion coefficient of O_2 in healthy tissue, values between $DO_2 = 3 \cdot 10^{-6}$ and $9 \cdot 10^{-6}$ cm^2/s are used, since the values given in the literature vary greatly. For comparison, $DO_2 = 3 \cdot 10^{-6}$ cm^2/s is given for intact cancer tissue, which is used as a basis in [163]. Because other papers [166, 167] assume $DO_2 \approx 9 \cdot 10^{-6}$ cm^2/s , we have also included this value in our consideration. Since we only need principles here, and not absolute values, the calculations have been extended over the whole range of variation of the DO_2 values.

d) The oxygen consumption in saturation is, according to the respiration characteristic (cf. Fig. 91), $PO_2 = 10$ ml/100 g · min and is in accordance with [164]. Depending on the demands on the functional capacity of the heart, other PO_2 values were also included in the calculation.

e) In accordance with [166] $R_c = 4$ μm was used for the outer capillary wall radius.

1.3.5 Calculation of the PO_2 distribution in the intercapillary space of normally supplied tissue

Figure 92 shows the calculation of the O_2 concentration dependent on the distance r of the capillary axis for normal tissue with the equation parameters named in Paragraph 1.3.4. The course of the curve for constant substrate consumption (area I, simplified calculation) is given, as is that for the diminishing substrate consumption below the saturation concentration (area II, accurate calculation as in [168]).

With reference to the supply, the level $PO_2 = 3.5$ mmHg (0.47 kPa) should be seen as the critical oxygen partial pressure, at which, according to [146, 164] the respiration of the cells changes to fermentation. An approximately normal supply thus exists as long as the condition $PO_2 > 3.5$ mmHg remains fulfilled in

the largest distances r occurring in the myocardium. The variation of r , which we use as a basis for healthy tissue, in accordance with [32, 166, 168, 169], is given in Fig. 92. It can be seen from the courses of the curves under what conditions the PO_2 reaches critically low levels in the tissue. The calculations given here represent the most unfavorable borderline case because of the underlying model with a single capillary. In reality the *contribution of neighboring capillaries to the O_2 supply* is always to be added. This additional contribution is especially prominent in the myocardium due to the relatively regular arrangement of the capillaries there. Figure 93 shows an idealized scheme of the capillarization of the myo-

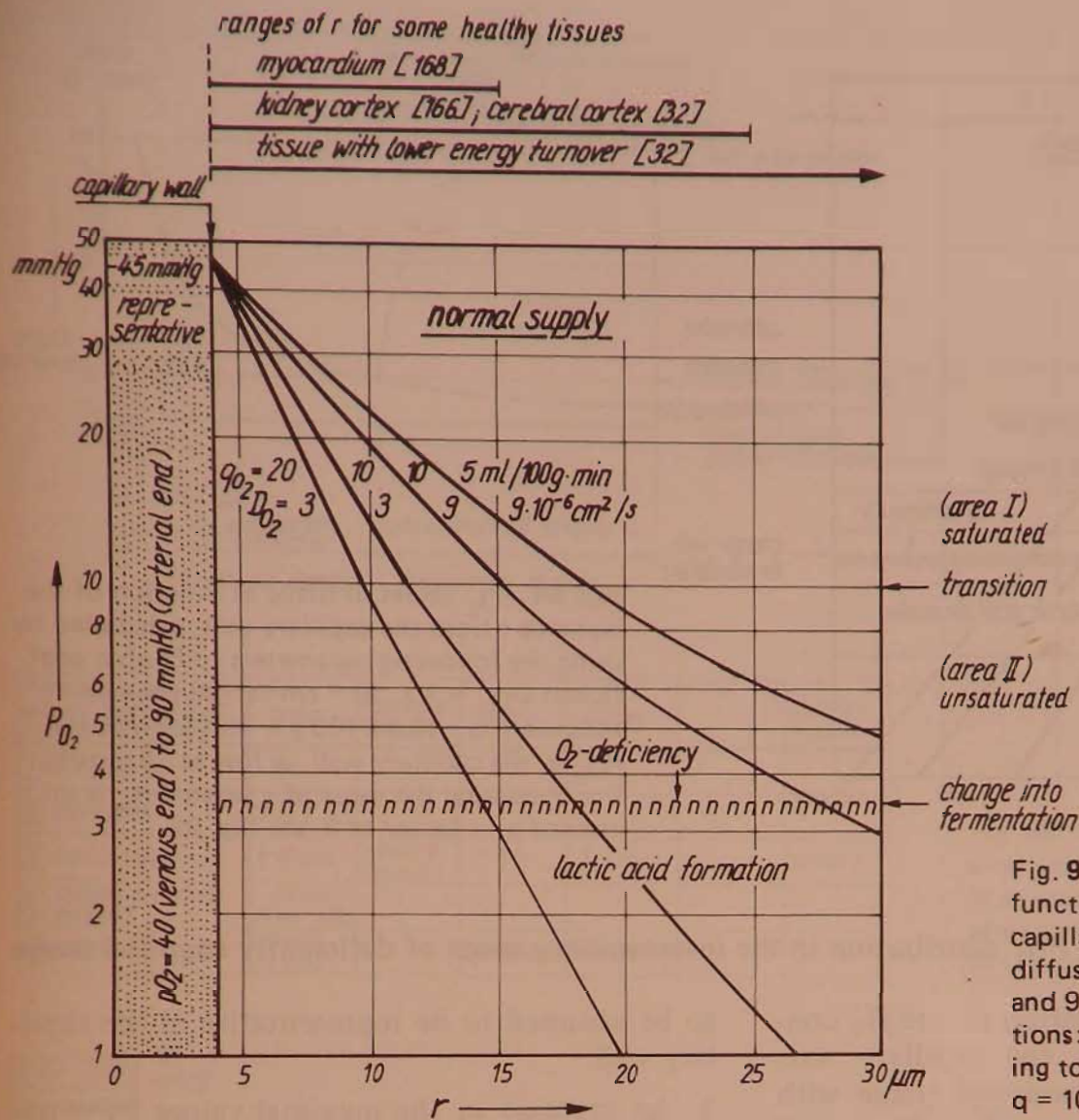


Fig. 92 P_{O_2} values in tissue as function of the distance r from the capillary axis, calculated for the diffusion coefficients $D_{O_2} = 3 \cdot 10^{-5}$ and $9 \cdot 10^{-6}$ cm²/s; further assumptions: healthy myocardium according to [163, 167]; O_2 consumption $q = 10$ ml/100 g·min (normal) as well as 20 and 5 ml/100 g·min

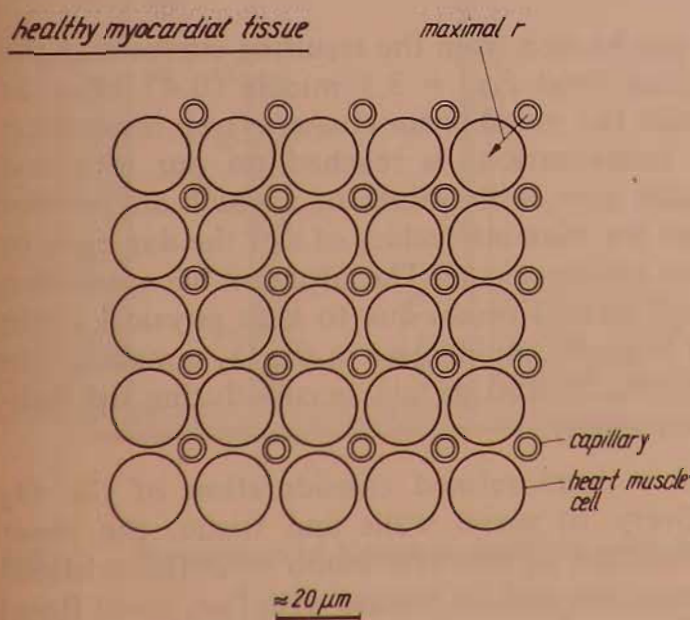


Fig. 93 Schematic capillary pattern of the myocardium. Idealized cross-section, modified according to [168]. On average one blood capillary is assigned to each heart muscle cell, so that every cell is supplied by four capillaries

cardium. According to this, each cell is supplied by four capillaries. The maximal nutritive distance, corresponding to the distance between capillary axis and myocardial cell, is entered above right in the scheme. In well-perfused myocardium under physiological conditions this value r is 15 μ m and more under pathological conditions (e.g. in structural dilatation). Because each cell is supplied by four capillaries, the drop in the P_{O_2} around the cell axis is smaller than in the mathematically simpler model of the diffusion field of a single capillary (for a means of calculation for the model with four capillaries, see [170]).

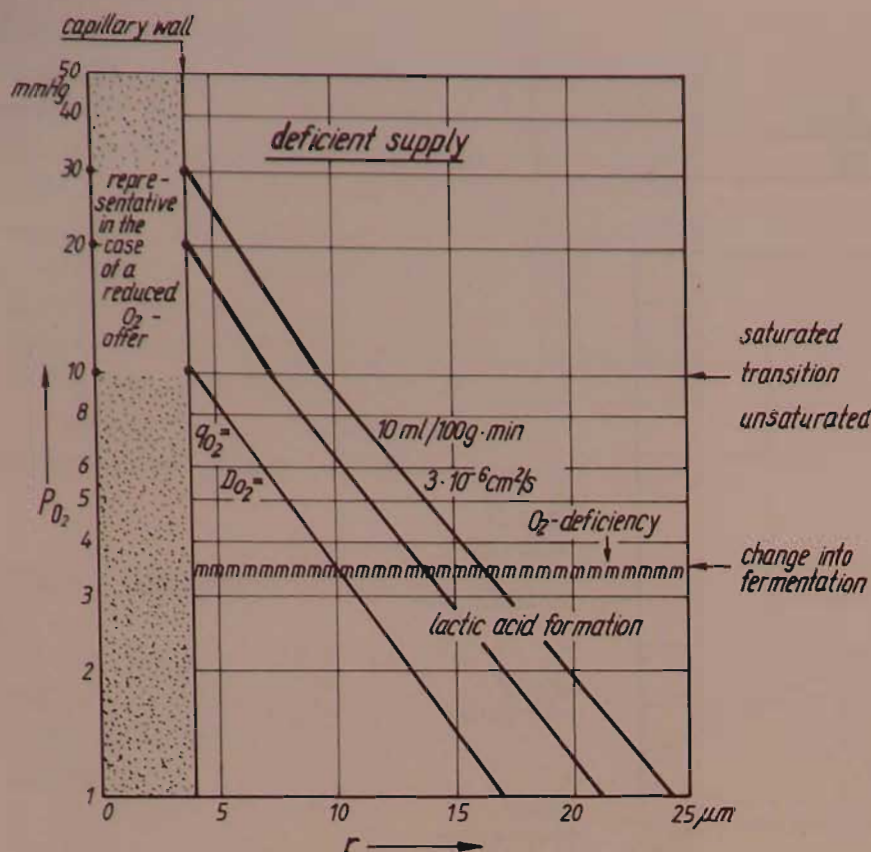


Fig. 94 P_{O_2} values in tissue as function of the distance r from the capillary axis, calculated by using the following parameters: diffusion coefficient $D_{O_2} = 3 \times 10^{-6} \text{ cm}^2/\text{s}$; oxygen consumption, $q \approx 10 \text{ ml}/100 \text{ g} \times \text{min}$ (normal); P_{O_2} at the capillary wall, as low as 30 mmHg. For increasing the value of r when D_{O_2} is increased by a factor of 3, see Fig. 92

1.3.6 Calculation of the P_{O_2} distribution in the intercapillary space of deficiently supplied tissue

Figure 94 shows the calculation of the O_2 concentration dependent on the capillary axis distance r for deficiently supplied tissue with the equation parameters named in Paragraph 1.3.4. The situation, which has drastically changed compared to Fig. 92, is a consequence of the numerical deterioration of three parameters in the case of deficient supply.

1. $P_{O_2} = 30 \text{ mmHg}$ (4 kPa) at the capillary wall is assumed as a representative level, when the O_2 offer is reduced. The variety of the factors which, individually or jointly, can cause the lower O_2 offer, have already been shown in their functional network [171].

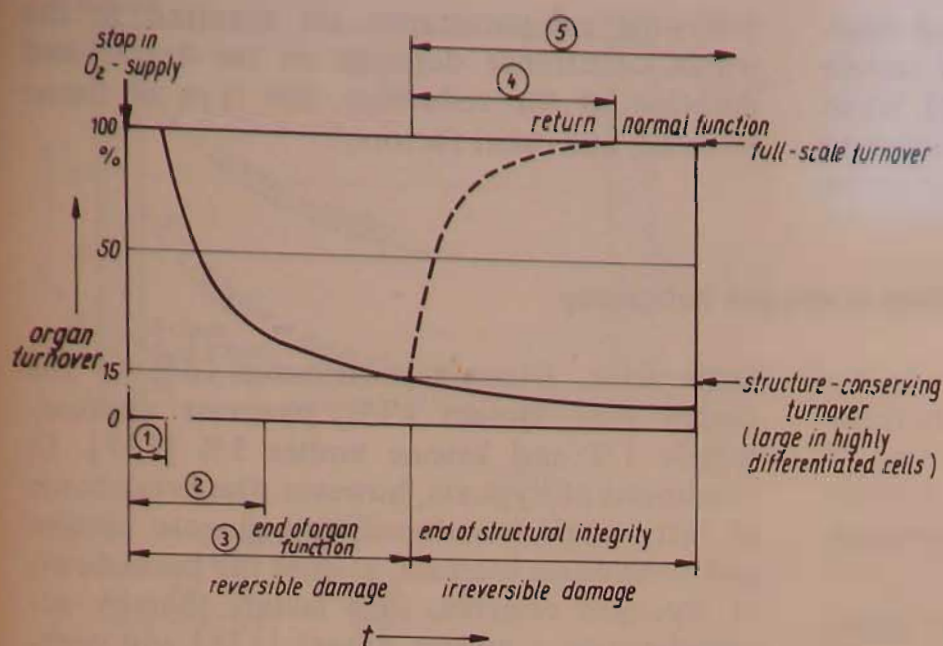
2. In severe circulatory disorders and in disorders of the microcirculation, as well as in the fast mesenchyme reaction after sclerogenic noxae, investigated by electron microscopic and also nuclear-physical methods [172], i.e. in vessels changed by arteriosclerosis, an additional severe deterioration in the capillary blood flow must be expected. In such cases, a P_{O_2} of between 30 and 100 mmHg (4.0 and 1.3 kPa) is

to be assumed to be representative in the capillary wall.

3. An increase in the maximal values for r occurs in structural dilatation.

It can be seen from the resulting curves that the critical level $P_{O_2} = 3.5 \text{ mmHg}$ (0.47 kPa), at which the metabolism changes from respiration to fermentation, is reached on our idealized model even with values of r which are smaller than the maximal values of r of the damaged or even healthy tissue. The situation becomes even more critical when, due to high physical strain for example, an increase in the O_2 consumption over $10 \text{ ml}/100 \text{ g} \cdot \text{min}$ occurs during the deficient supply.

For a more refined consideration of the O_2 delivery to vessel walls and tissue, the *inner convection of the red blood cells* (intensified) convection and O_2 release with fast blood flow) and the *hemodynamics* (e.g. formation of turbulences) must also be taken into account [173].



characteristic time intervals for reversible and irreversible damage	brain	myocardium	liver	kidney	skeletal muscle
① symptom free	4 s				
② paralysis	8-12 s				
③ reactivation	8-10 min	several h (at rest)	3-4 h	3-4 h	several h
④ latency period for recovery	10 min (4 min stop)				
⑤ recovery	hours to days		several days	several days	

Fig. 95 Behavior of cellular turnover after stop in O_2 supply [32]. Broken line: recovery of cellular turnover after early enough release of the stop in O_2 supply

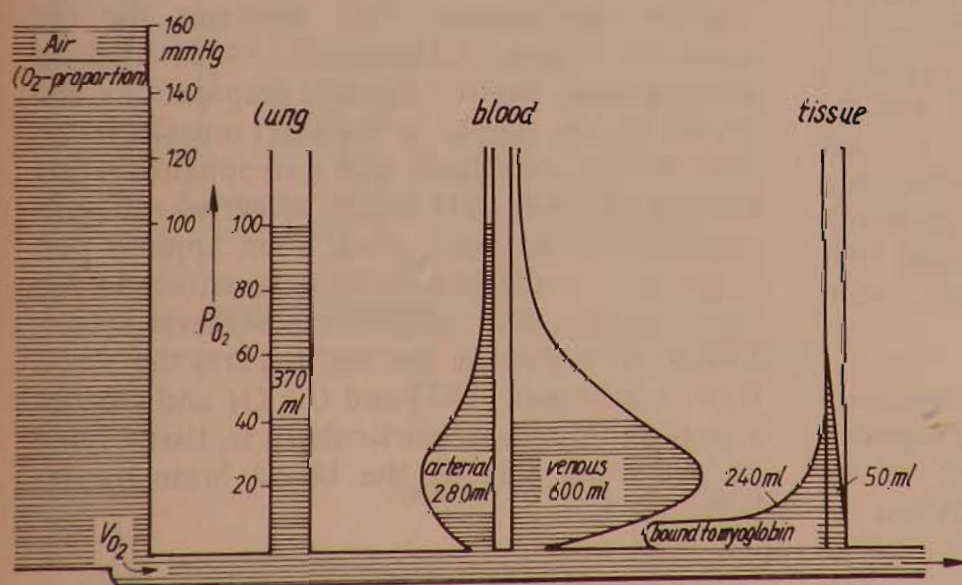


Fig. 96 Scheme of the oxygen distribution in the human body [174]. The O_2 is presented as fluid, the height of which indicates the partial pressure in the respective reservoir. The arterial blood in the pulmonary vein, the left heart and in the arterial system, contains ca. 280 ml. The venous blood still includes a mean of 600 ml (!). The myoglobin binds approximately 240 ml, whilst the lung on average contains another ca. 370 ml

1.4 Reactions in tissue to local oxygen deficiency

1.4.1 Reversible and irreversible cell damage

After a short *symptom-free interval*, in which the cell function remains in full, every total stop in O_2 supply causes *damage* which is at first *reversible* but which soon causes the *organ function to cease* and the *structure to disintegrate*. If the O_2 supply re-occurs before the structural disintegration, the organ function returns, as in Fig. 95. If this timepoint is exceeded, *irreversible damage* occurs.

Figure 96 shows a scheme of the distribution of the O_2 content in the body. Theoretically the whole oxygen would be consumed in approximately 5 min with a resting O_2 consumption rate of 300 ml/min.

In the application of the O_2 MT we are usually dealing with a *weakened O_2 supply* and not with a total interruption. Just a few types of

application with a spatially very limited interruption in O_2 supply (the occlusion of certain blood vessels form an exception to this). When the oxygen supply is weakened, the extent to which the reaction mechanism discussed in the

following sub-paragraphs are involved in the whole occurrence depends on the degree and duration of the reduction, the type of tissue affected, and other factors.

1.4.2 Energy gain by means of glycolysis in oxygen deficiency

The individual cell in the organism needs, for the maintenance of its structure and its readiness and ability to perform its function, a certain energy supply, which it mainly obtains from the *oxidative catabolism of nutrients*, when the O_2 offer is sufficient.

When the oxygen is lacking (anaerobic condition) the required energy can simply be gained by *glycolysis*. Under in vivo conditions the oxidative breakdown of 1 mol glucose delivers 689 kcal (2885 kJ) and is connected to the formation of 38 mol ATP. With 270–380 kcal (1130–1590 kJ) these represent the (physiologically) utilizable free energy which corresponds to an energy yield of between 39 and 55%. By comparison, the transformation of 1 mol glucose into 2 mol lactate is connected with a reaction energy of only 47 kcal (196 kJ), by which 2 mol ATP are formed. These correspond to only 16–20 kcal (67–84 kJ) and an energy yield of 3.4–4.3%. Thus the aerobic decomposition of glucose supplies a total amount of energy which is 15 times higher, and ATP which is 19 times higher, than glycolysis [175, 176]. It is therefore not surprising that the end-product of the glycolysis, lactic acid, still contains a high amount of energy.

Special relationships exist in the heart inasmuch as the heart muscle which is sufficiently supplied with oxygen, covers more than 50% of its energy requirements from the oxidation of

fatty acids. Glucose contributes 18% to the energy gain, lactate 17%, pyruvate approximately 1% and ketone bodies 5% [177]. In conditions of hypoxia, however, the breakdown of fatty acids is reduced, and glucose uptake and breakdown increase, as does the breakdown of glycogen reserves; thus lactate thereby accumulates to a greater extent [178] and overacidification occurs. The joint use of the lactic acid as an energy substrate in the myocardium (and perhaps also in the brain with a contribution of glycolysis to metabolism of approximately 19%), can be strengthened by g-strophanthin [169, 179–182]. This effect is indicated by an increase in the pH in O_2 -deficient areas of the myocardium, roughly 3 min after administration of g-strophanthin. This increase is found only with g-strophanthin, not with digitalis preparations. This confirms the old concepts (Sarre, Uhlenbruck 1953) that g-strophanthin, but not digitalis preparations, improves the O_2 supply to the heart muscle. It has been hardly considered that g-strophanthin (according to [148, 183], highly effective and with reproducible potency, even when applied perlingually), in addition to its main effect in the heart muscle, also triggers a peripheral effect. Due to its action on the vasculature, the blood flow is increased [185] and the O_2 and glucose supply is improved, particularly in tissue lying on the other side of the blood brain barrier [186, 187].

1.4.3 Target area in tissue for O_2 deficiency and O_2 MT

The calculations of the dependence of the oxygen partial pressure PO_2 on the distance r to the capillary axis in the single-capillary model (Fig. 92) referred to the PO_2 level (e.g. 45 mmHg) existing in the centre of the capillary. In reality the PO_2 drops, under normal conditions, from the arterial to the venous end of the capillary from 93 to 63–23 mmHg, depending on the organ (cf. Fig. 9). For an example roughly corresponding to skeletal muscle, curve A in Fig. 97 shows the course of the PO_2 along the capillary, and curve B the course of the coaxial cylinder area of the distance $r = 30 \mu m$. The presentation shows

that the *tissue area most at risk from O_2 deficiency is localized at the venous end of the capillary and at a great distance r from the capillary axis*. Under normal conditions the relative frequency is $f < 2\%$ for $PO_2 < 3.5$ mmHg (change to fermentation metabolism), and $f < 0.2\%$ for $PO_2 < 1$ mmHg (critical PO_2 of the mitochondria, irreversible cell damage), as can be roughly seen from the distribution curve in Fig. 98.

The tissue area with high values of r at the venous end of the capillaries ("lethal corner") as discussed, forms, as can be seen in Fig. 99,

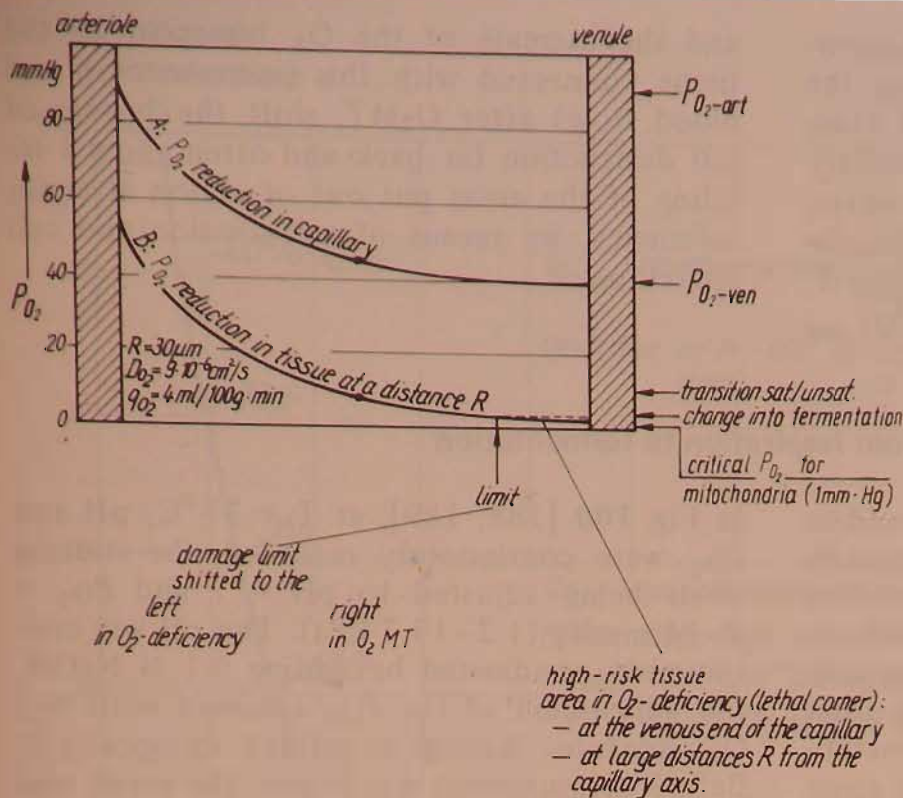


Fig. 97 P_{O_2} Topography in the tissue between the arterial and venous ends of the nourishing capillaries. Example. Presentation of the target area for O_2 deficiency and O_2 MT at the venous end of the nourishing capillaries. 1 mmHg = $1.33\cdot 10^2$ Pa

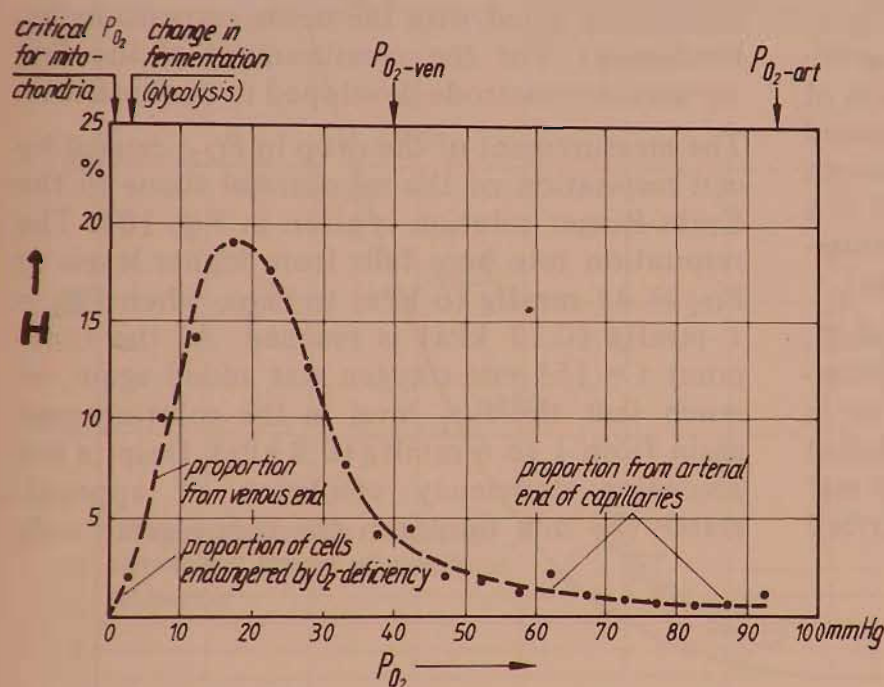


Fig. 98 Relative frequency H of the O_2 partial pressure in the cerebral cortex of guinea-pigs under normal conditions. Modified according to measurements in [32]. 1 mmHg = $1.33\cdot 10^2$ Pa

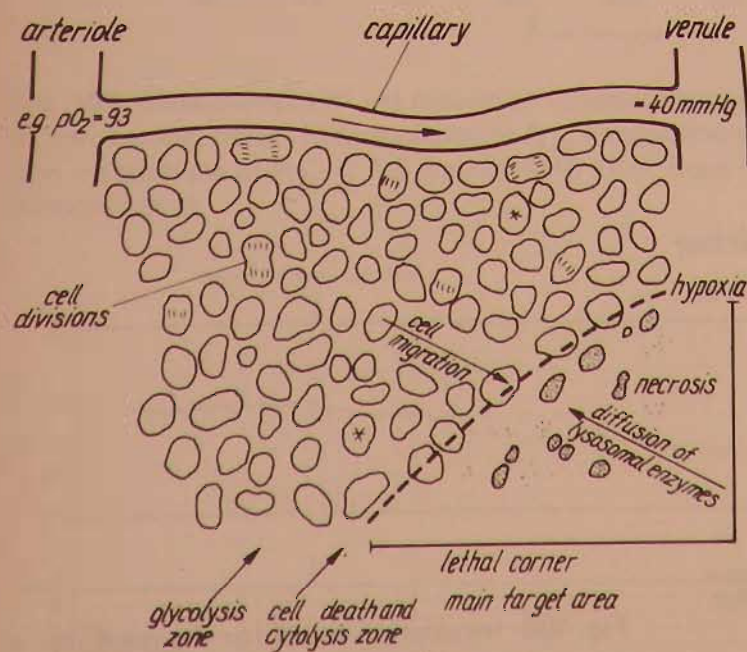


Fig. 99 Idealized model of the main target area of O_2 MT in the intercapillary space. 1 mmHg = $1.33\cdot 10^2$ Pa

the microspaces of the organism, where the destruction of cells is initiated, or occurs, and where an energetic limit is set on growth in the intercapillary space.

In the brain, where no new nerve cells are formed and where an established network exists between the cells, this spatial relation has a strongly definitive character. For this reason, too, a disorder in the formed microstructure has greater consequences than in other organs (concussion).

Here the cell loss occurs, by which for example, the body of the ageing individual tries to adapt itself to the increasing deterioration in the O_2 supply to its tissue (drop in cardiopulmonary performance with age). At this site in the intercapillary space such high rates of cell loss finally develop in organs that O_2 deficiency

diseases are triggered. At the same site, however, there is also a *main effect area* of the O_2MT . An improvement in the deficient situation in the venous supply area of the capillary by means of raising the PO_{2-art} is, however, strictly limited, because this rise benefits the arterial area of the capillary more by far (cf. Fig. 3). But the lasting drop in the PO_{2-ven}

and the increase of the O_2 transport to the tissue connected with this (increase of η and blood flow) after O_2MT , shift the border of cell destruction far back and often allow a re-filling of the areas put out of action after O_2 deficiency, by means of cell division and cell migration.

1.4.4 Change in the cell metabolism from respiration to fermentation

In increasing O_2 deficiency the cell is forced to cover its energy deficit by glycolysis (Paragraph 1.4.2). Due to the energy yield of fermentation metabolism being only 7% compared with respiration, glycolysis increases very quickly below a certain PO_2 level. It is therefore usual to speak of a sudden change in the cell metabolism. In [146] $PO_2 = 5 \text{ mmHg}$ (0.6 kPa) is given as a critical level for the change from respiration to fermentation. Because of the significance of this figure for the over-acidification of tissue areas affected by O_2 deficiency, discussed in the following paragraph, it seemed worth determining directly the critical PO_2 level in a specially constructed PO_2/pH *in vitro* measurement arrangement with high sensitivity [146].

For this the hearts of 1 to 2-day-old, or adult, rats were homogenized in an ice-cold bicarbonate-free Krebs-Ringer solution (KR) or in lactalbumin-yeast medium (LY), and incubated in the named solutions containing 200–100 mg/100 ml glucose in vessels of the type described

in Fig. 100 [188, 189], at $T = 37^\circ\text{C}$; pH and PO_2 were continuously recorded, the starting levels being adjusted to $pH = 7$ and $PO_2 = 9\text{--}14 \text{ mmHg}$ (1.2–19.7 kPa). The pH was continuously re-adjusted by adding 0.1 N NaOH, the adjustment of the PO_2 achieved with N_2/O_2 mixtures having a defined composition. Before measurement was begun, the vessel was completely filled with the tissue suspension (no headspace). For the measurement of the PO_2 we used an electrode developed in our institute.

The measurement of the drop in PO_2 , caused by cell respiration of the myocardial tissue in the Krebs-Ringer solution is given in Fig. 101. The respiration rate here falls from higher levels at $PO_2 = 45 \text{ mmHg}$ (6 kPa) to zero, when $PO_2 = 1 \text{ mmHg}$ (0.13 kPa) is reached. At the time-point $t = 155 \text{ min}$ oxygen was added again, so much that the PO_2 level in the solution rose again from 1 to 6 mmHg (0.8 kPa). Despite the preceding deficiency condition of approximately 20 min duration, the myocardial cells

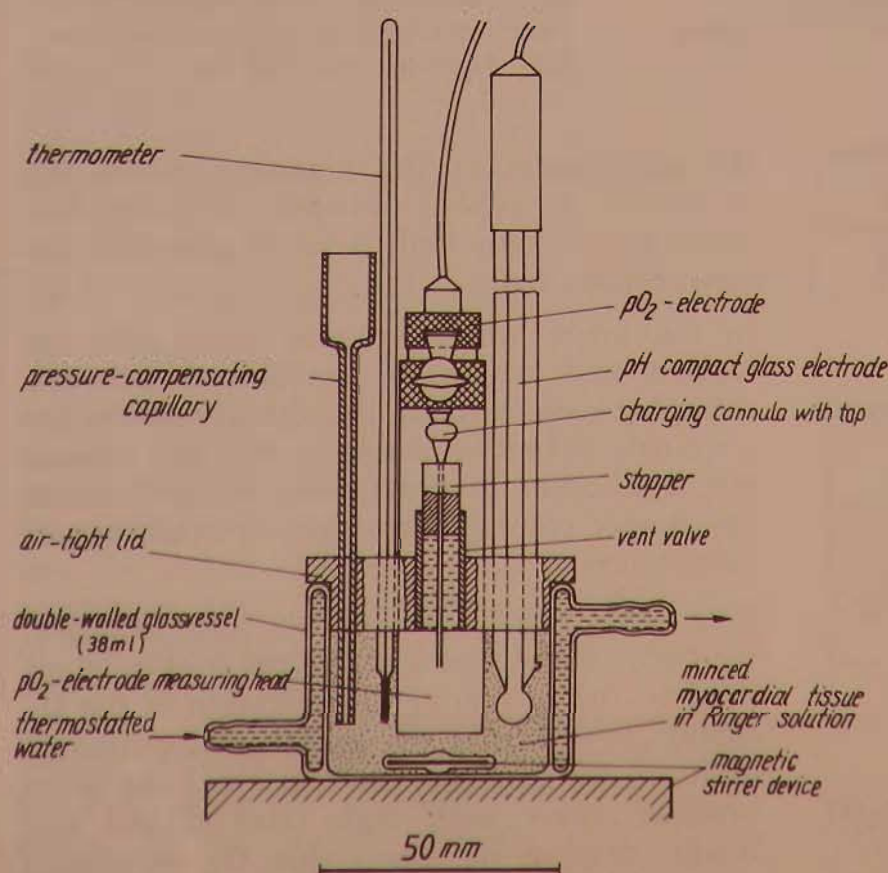


Fig. 100 Incubation vessel for the measurement of respiration and acidification (glycolysis) of myocardial cells as a function of the PO_2 level

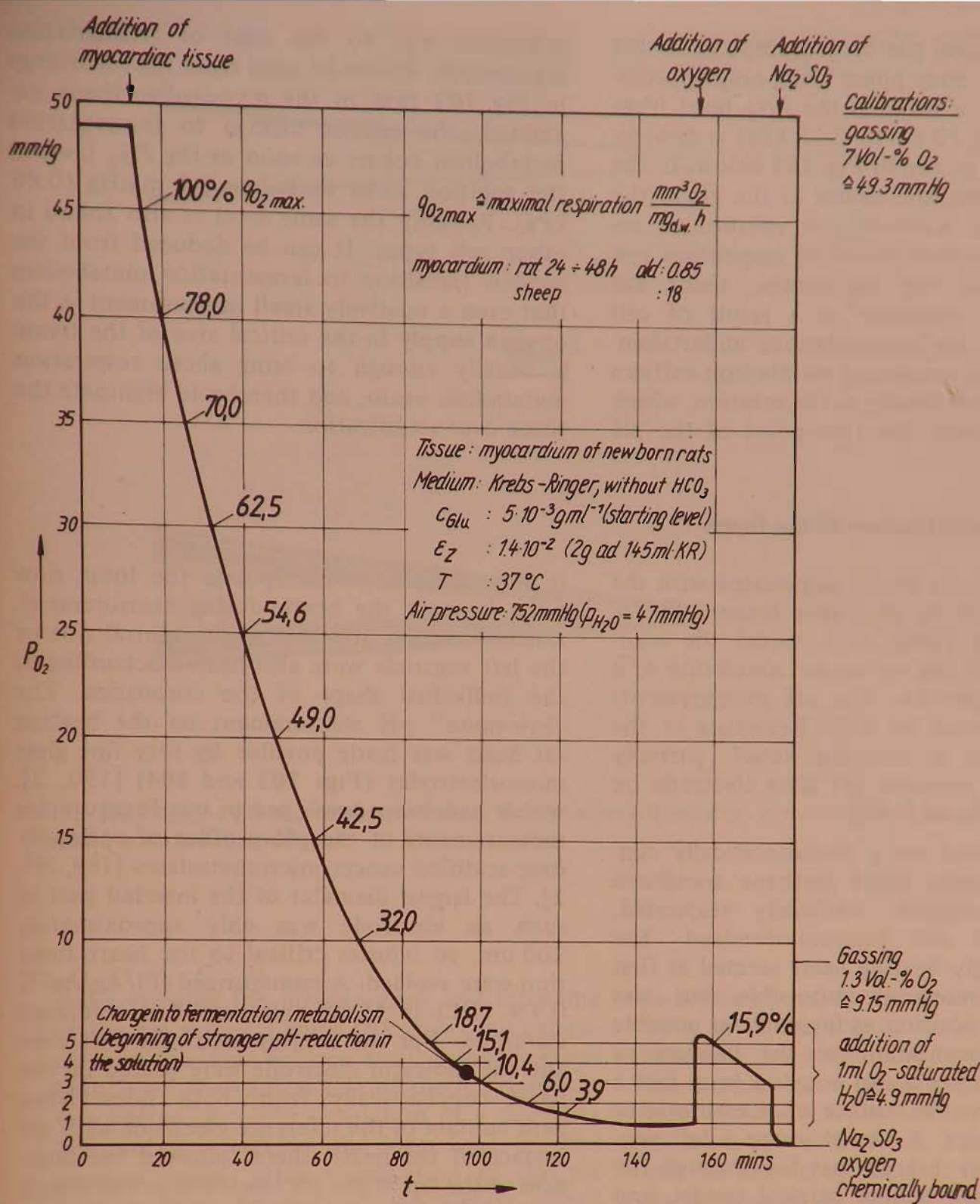


Fig. 101 Measurement of pH reduction (conditioned by cell respiration) of a Krebs-Ringer solution after addition of myocardial tissue. Electrochemical P_{O_2} measurement using the Clark electrode. Result: change into fermentation metabolism at $P_{\text{O}_2} \leq 3.5 \text{ mmHg}$ (0.46 kPa). Stop in respiration at $P_{\text{O}_2} \leq 1 \text{ mmHg}$ (0.13 kPa) (critical P_{O_2} for mitochondria)

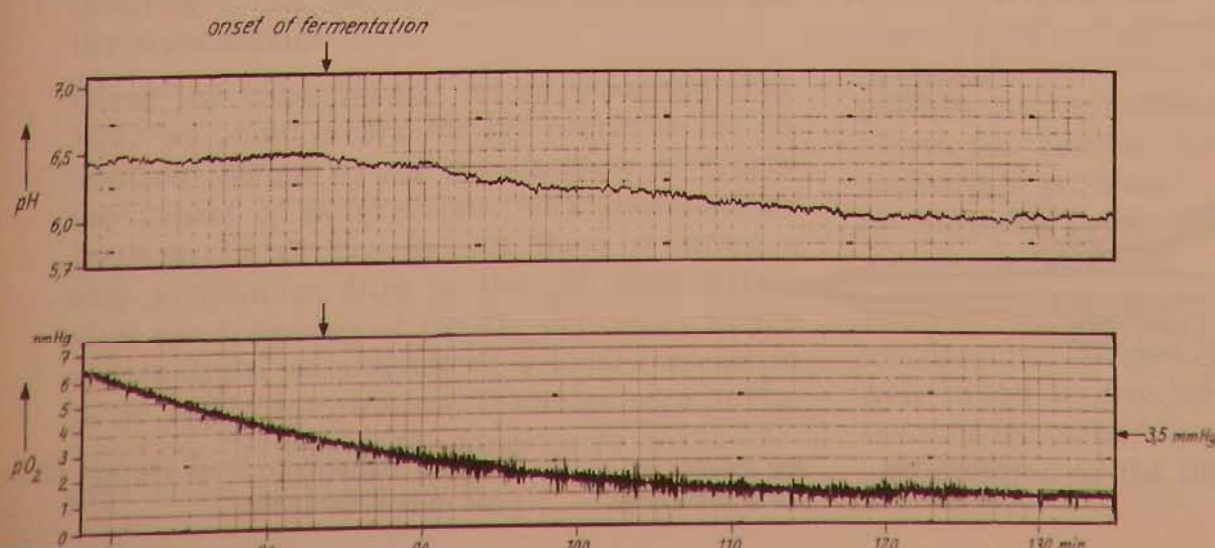


Fig. 102 Simultaneous registration of pH and P_{O_2} in Krebs-Ringer solution after addition of myocardial tissue from 24–48-h-old rats. Result: Change in fermentation metabolism after reduction of the P_{O_2} to $\leq 3.5 \text{ mmHg}$ (= 0.46 kPa), caused by cell respiration

then respired again, the drop in respiration rate due to the deficiency phase being only approximately 13 %. The drop in the P_{O_2} level from 6.5 to 1 mmHg (0.87 to 0.13 kPa) is directly reflected in the record in Fig. 102 below. In the same figure above, the course of the pH in the bicarbonate-free Krebs-Ringer solution is recorded. The absolute values of respiration and fermentation of the myocardial tissue are relatively low, evidently as a result of cell damage due to the manipulations undertaken. Despite this, the remaining metabolism suffices to allow us to see clearly in the solution, which is kept buffer-free, the time-point of the pH

reduction due to the start of fermentation metabolism. It can be seen from the recordings in Fig. 102 that in the myocardial tissue examined, the sudden change to fermentation metabolism occurs as soon as the P_{O_2} level in the solution sinks to below 3.5 mmHg (0.46 kPa). Roughly the same level is also found in other cell types. It can be deduced from the sudden transition to fermentation metabolism that even a relatively small improvement in the oxygen supply in the critical area of the tissue is usually enough to bring about respiration metabolism again, and thereby to eliminate the tissue over-acidification.

1.4.5 Over-acidification of the tissue

In order to become better acquainted with the over-acidification by glycolysis (caused by O_2 deficiency), we chose as a model the *myocardial tissue of the rat under simulation of a myocardial infarction*. The pH measurements were implemented by P.G. Reitnauer in the supply area of a coronary vessel, partially ligated, with a movable pH glass electrode on the beating rat heart [146].

Wistar rats placed on a thermostatically controlled stage under ethyl urethane anesthesia were tracheotomized, artificially respired, thoracotomized and pericardiotomized. The exposed, strongly beating heart seemed at first to make measurement impossible, but was brought into a position as favorable as possible for the implementation of the ligature or measurement, by placing a nylon loop just a little way below the surface of the outermost apex of the heart. A thread under a left ventricular coronary branch was fed through the myocardium with a bent surgical needle, and made into a loose loop, in order to trigger later an experimental myocardial infarction. In order to throttle the large vascular trunks, the heart had to be turned upwards and the ligature positioned on its dorsal side. However, since

it was difficult to manipulate the loop, now lying beneath the heart, during measurement, smaller vascular branches of the ventral side of the left ventricle were also ligated according to the individual shape of the coronaries. The "low-noise" pH measurement on the beating rat heart was made possible by very fine glass microelectrodes (Figs 103 and 104) [190, 2], which had been developed in our Institute for measurements of the pH profiles of optimally over-acidified cancer micrometastases [189, 191, 2]. The largest diameter of the inserted part of such an electrode was only approximately 200 μm , so injuries critical to the heart function were avoided. A miniaturized (Pt/Ag/AgCl/0.9 % NaCl in H_2O) unit served as reference electrode. For the measurement the reference and the indicator electrode were placed on the heart concentrically from both sides. After firm contact of the reference electrode with the surface of the heart, there followed the insertion of the tip of the pH electrode in the supply area of the coronary vessel branch prepared for the ligature, approximately 1 mm deep in the myocardium. The position of the heart was stabilized by the three points of contact, apex loop, reference and pH electrodes, enough to

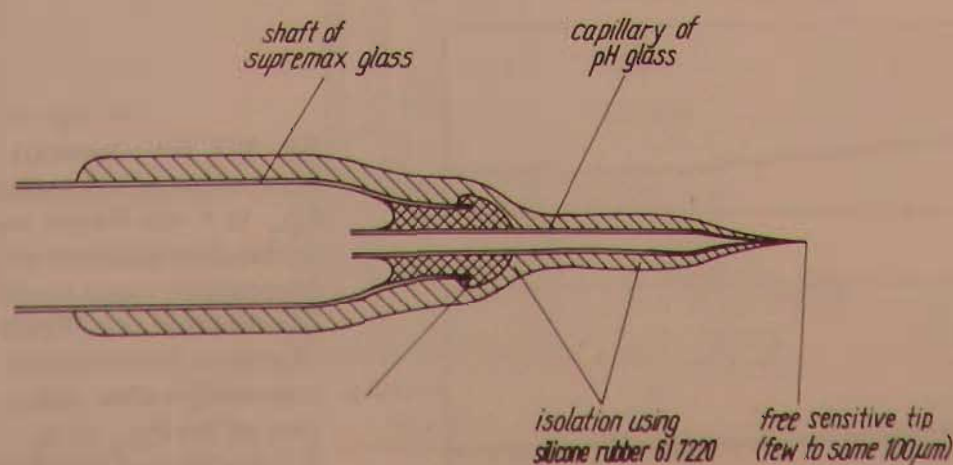


Fig. 103 Schematic cross-section of a pH micro-electrode

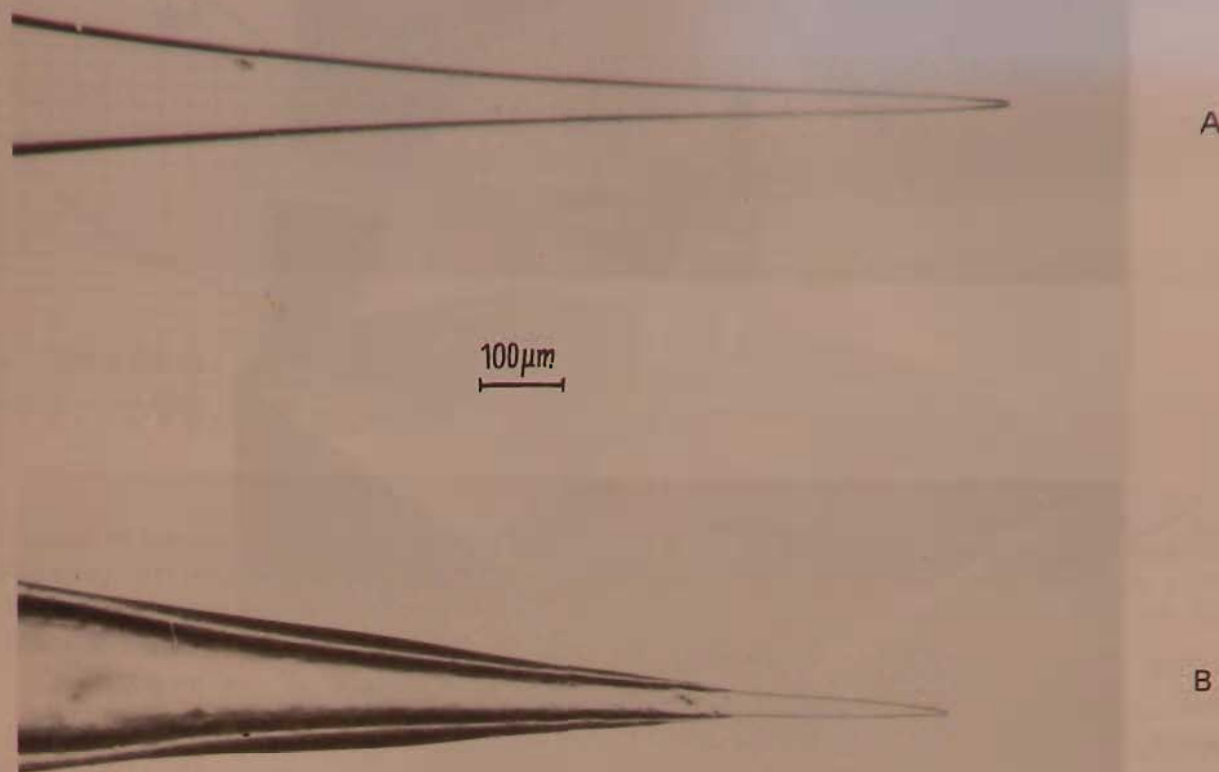


Fig. 104 Tip of a pH microelectrode before (A) and after (B) isolation with silicone rubber (free length of the sensitive tip is a few 100 μm)

make possible the measurement and recording of the pH values. Figure 105 shows this experiment in the stage before a small coronary vessel branch on the ventral side of the left ventricle was ligated. For the simulation of a coronary myocardial infarction, the loop used for this purpose could, after stabilization of the pH starting level, be more or less tightly pulled together using two pairs of tweezers and avoiding any further influence on the position of the heart; the loop could also, if necessary, be loosened again at a desired moment, by inserting a fine needle between the thread and the myocardium.

Using the experimental set-up discussed (Fig. 106) we could record the pH course in the O_2 deficient region of the myocardium of rats in the course of an experimentally generated infarction. In all experiments there occurred a very substantial drop in the pH immediately after the triggering of the O_2 deficiency in the myocardium, as a result of a local increase in lactic acid concentration. It can be seen in Fig. 106 how the P_{O_2} in the supply area of the relevant vessel sinks by $\Delta\text{pH} = 1$ within 2 min,

immediately after the constriction of a coronary vessel branch of the left ventricle. As a result of the incomplete ligature and a remaining supply from other sources (collateral vessels, diffusion from the environment), there occurs a pH level of 6.2. The remaining supply can be proven by the fact that, when artificial respiration of the animal is stopped, the pH immediately drops further and then reaches a level of 5.2 within 16 min. This also shows how fast and how low the pH in the myocardium must drop and cause damage to the tissue (microcirculation inhibition, vascular "porosity", increase in red cell aggregation, release and activation of the lysosomal enzymes, cytolytic chain reaction etc.) when, as can be expected in larger hearts (in humans for example), the infarct mechanism proceeds in such a way that there is no remaining supply from the environment.

The method of pH registration in a tissue area temporarily brought under O_2 deficiency is well suited to give information as to whether the damage caused by weakened supply (degree and duration of the impairment) is of a reversi-

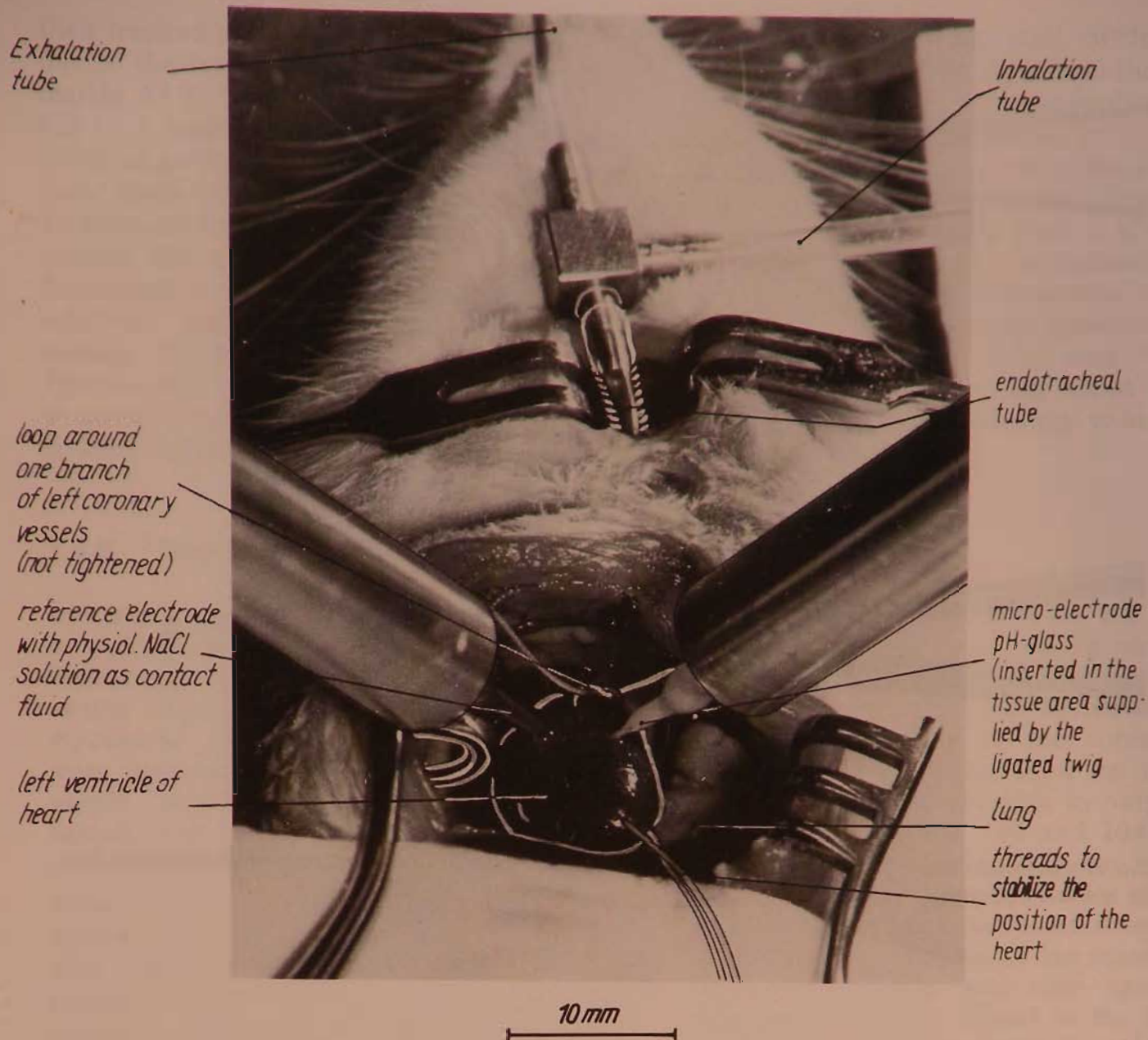


Fig. 105 pH measurement in myocardium of the left ventricle of a rat, under conditions simulating an infarct. Tracheostomy, thoracotomy, pericardiostomy, artificial respiration. Measurements on the beating (fixed) heart using a glass microelectrode having a pH-sensitive tip of $100\ \mu\text{m}$ length [146] were done as smoothly and tissue-protectively as possible

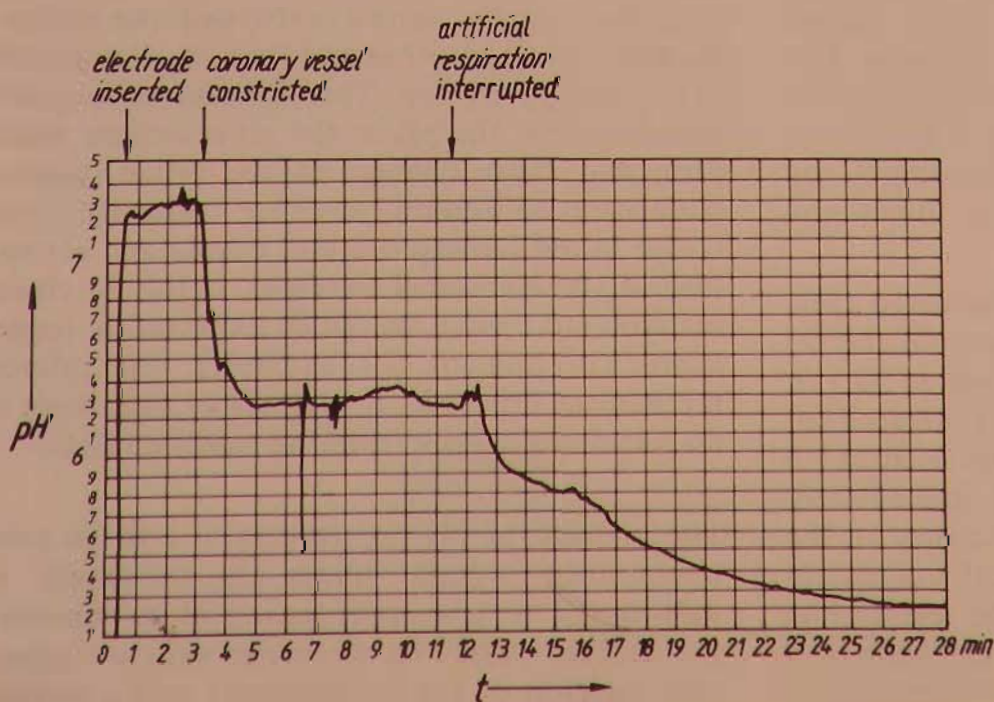


Fig. 106 In vivo pH registration using glass micro-electrodes in the myocardium of the left ventricle of a rat after generation of O_2 deficiency by constriction of coronaries (pH minimum = 6.25) and by cessation of artificial respiration (pH minimum = 5.25); $T = 37^\circ\text{C}$ [146]

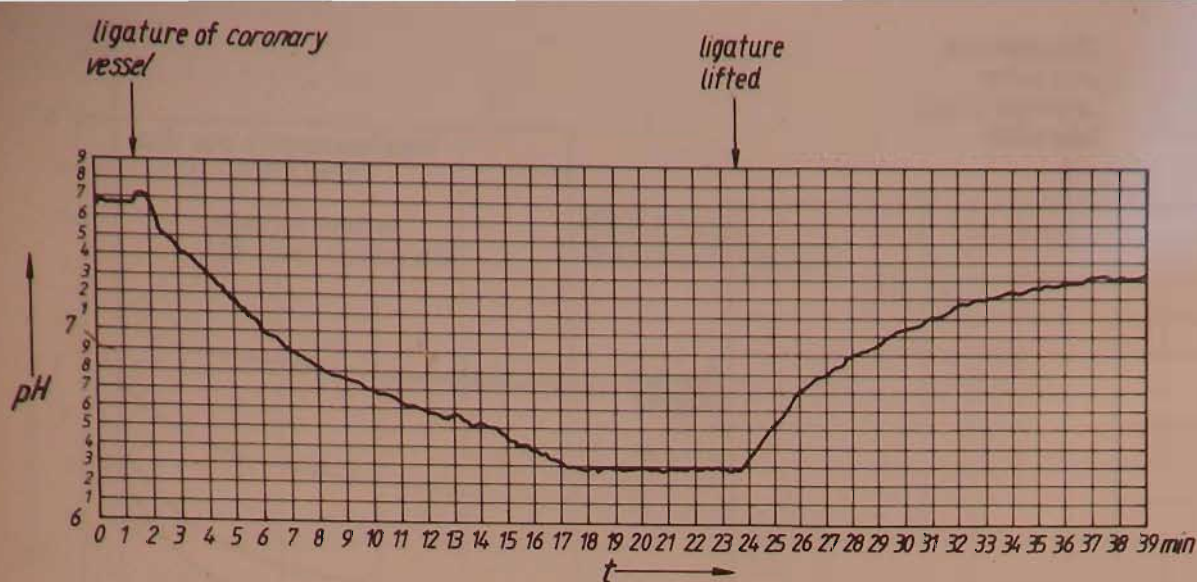


Fig. 107 pH course in the myocardium of the left ventricle of a rat, showing the reversibility of tissue impairment due to O_2 deficiency: pH renormalization after lifting the vascular occlusion as indicator. In another experiment of this type the blockade was not lifted after $t = 24$ min, but only after $t = 50$ min, and did not return to normal (irreversible tissue damage, stop in microcirculation)

ble or irreversible nature (cf. Fig. 95 above). Figure 107 shows an example of this. In this registration the pH drops from 7.7 to 6.3 after the vascular constriction, i.e. by 1.4 pH units, and quickly rises again to a normal level (7.3) after the vessel narrowing is lifted 22 min later. This shows how irreversible damage can be prevented and the metabolism of the tissue restored, by eliminating early enough the disturbance of supply. *The restoration of the pH in the affected tissue area after the removal of the disturbing factor can be regarded as an indicator of the still reversible nature of the damage.*

The duration of the phase in which the damage is still of a reversible nature (e.g. 25 min in myocardial infarction) is, according to WHO statistics, only in 5% of all cases longer than the time until the start of emergency medical care. It necessarily follows from this that only the patient himself (informed, prepared and supplied with fast-acting drugs and, if necessary, also equipment) can aid himself effectively. *When risk factors exist, it is therefore one of the most pressing duties of the physician dealing with the case to equip the high-risk patient so that the danger of irreversible O_2 deficiency damage is minimized* (e.g. with the emergency package of "Strodival special", Fig. 87, and, if necessary, also with 0.5 g methylprednisolone for risk of myocardial infarction, or with an oxygen carrier bag device for risk of stroke etc.). When irreversible damage has already occurred, the natural timepoint for particularly effective counter-measures has passed.

O_2 deficiency can have the most varied causes. One of these causes is an inadequate anesthesi-

zing technique (intensity and duration). The measurement in Fig. 108 shows the fast, substantial drop in the pH in the cerebral cortex during the death of a rat, caused by an overdose of ether [2, 191]. We are dealing here with a very complex process, occurring in a larger confluent tissue area, a process in which not only O_2 deficiency in the nerve tissue, but also the *deficient situation* and thereby labilization of the blood-brain barrier [192], must play a role (see also Paragraph 1.4.10).

Connection between volume of the O_2 -deficient tissue and amount of over-acidification. In the experiment in Figs 105 and 106 the volume of the O_2 -deficient region in the myocardium is $V \approx 10 \text{ mm}^3$ (supply area of the narrowed coronary vessel) after 3–12 min. The pH drops to approximately 6.25. After $t = 12$ min, i.e. after termination of artificial respiration, the deficiency volume spreads over the whole heart, and a further steep drop in pH can be detected in the registration. This finding leads us to the question of the influence of the volume of the tissue affected by O_2 deficiency on the size of the pH reduction.

Because the lactic acid formed by fermentation is quickly drained off the cell, the intracellular pH of a single glycolyzing cell hardly drops below the level of the environment [191]. However, overacidification increases rapidly with increasing volume V of the cell conglomeration, as can be seen from measurements on micro-metastases of different size [191]. The relationship between pH drop and volume of micro-metastases consisting of almost 100% of glycolyzing tumor cells at a constant blood glucose level of $4 \cdot 10^{-3} \text{ g/ml}$ is given by the

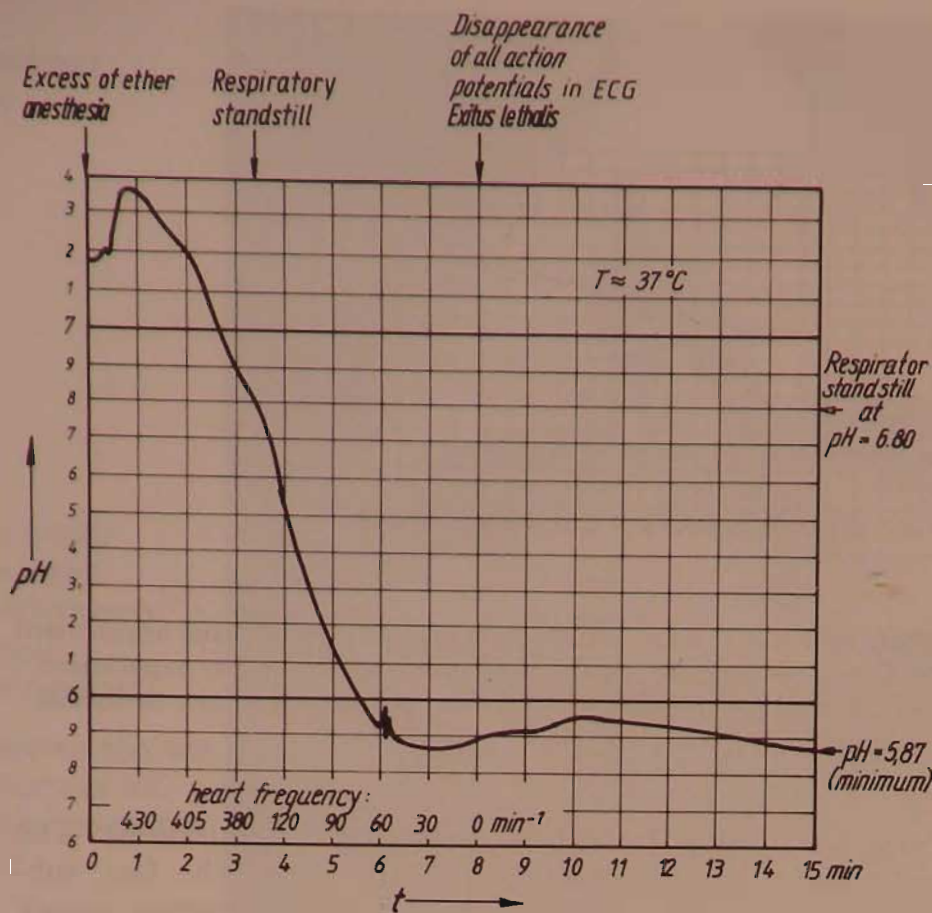


Fig. 108 Recording of the pH in the cerebral cortex of a rat in the pre-final and final stage of prolonged ether anesthesia at a normal blood glucose level. Result: a spontaneous, rapid drop of cerebral pH leads to exitus letalis within ≈ 6 min

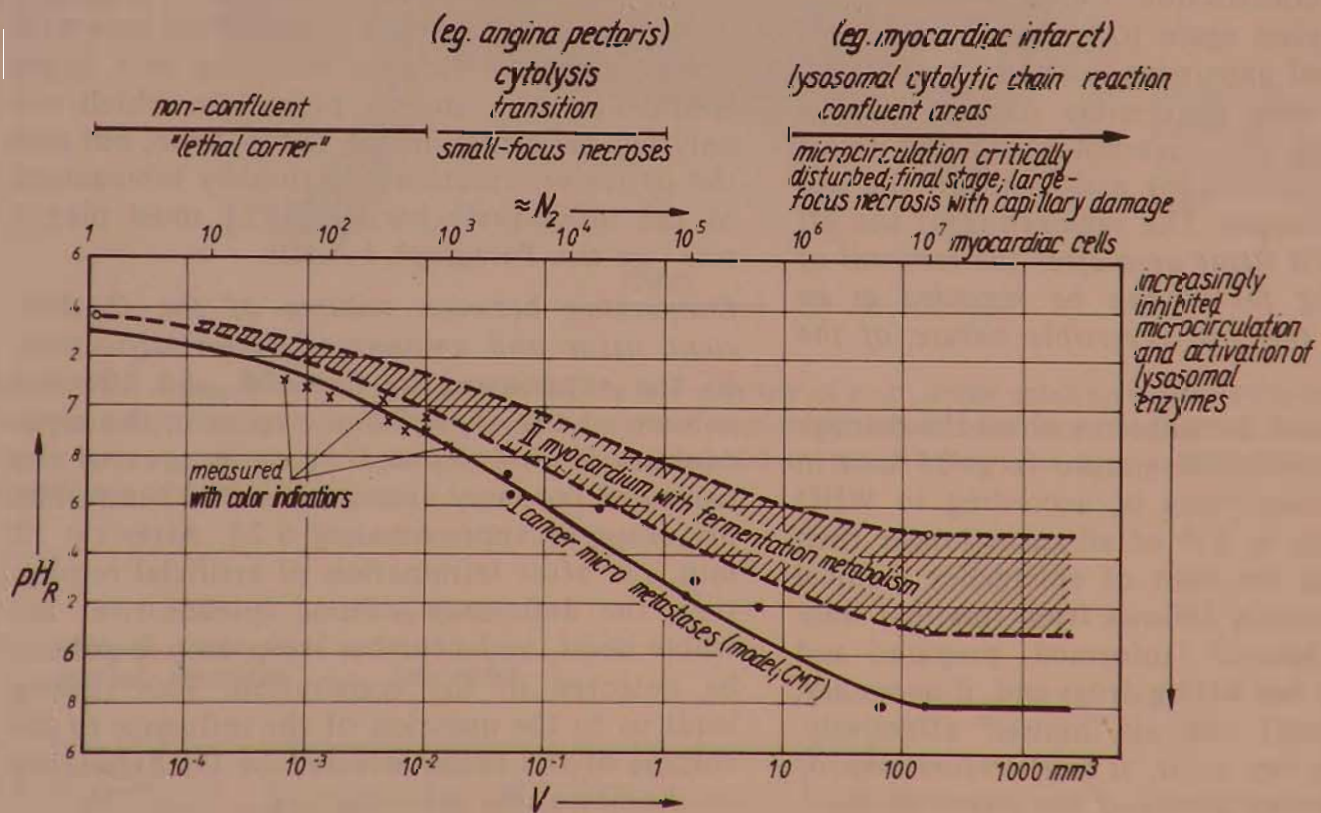


Fig. 109 Guidelines for the dependency of the tissue pH on the size of volume V with total O_2 deficiency. Measurements on cancer micro-metastases as models for glycolyzing tissue, with glass micro-electrodes under CMT conditions [2, 191]; $V \approx$ volume with O_2 utilization deficit

solid line in Fig. 109. We must allow for a normal blood glucose concentration for our problem (except for badly stabilized diabetics, see below). Different fermentation capacity and supply situation of the cells as well as other metabolic exchange rate constants are also

given. Our model can therefore only give an approximate idea of the functional connection. It should nevertheless supply sufficient relevant guiding values for the pH reduction with growing O_2 -deficient tissue volume, because we had pH measurements for the extreme cases of the

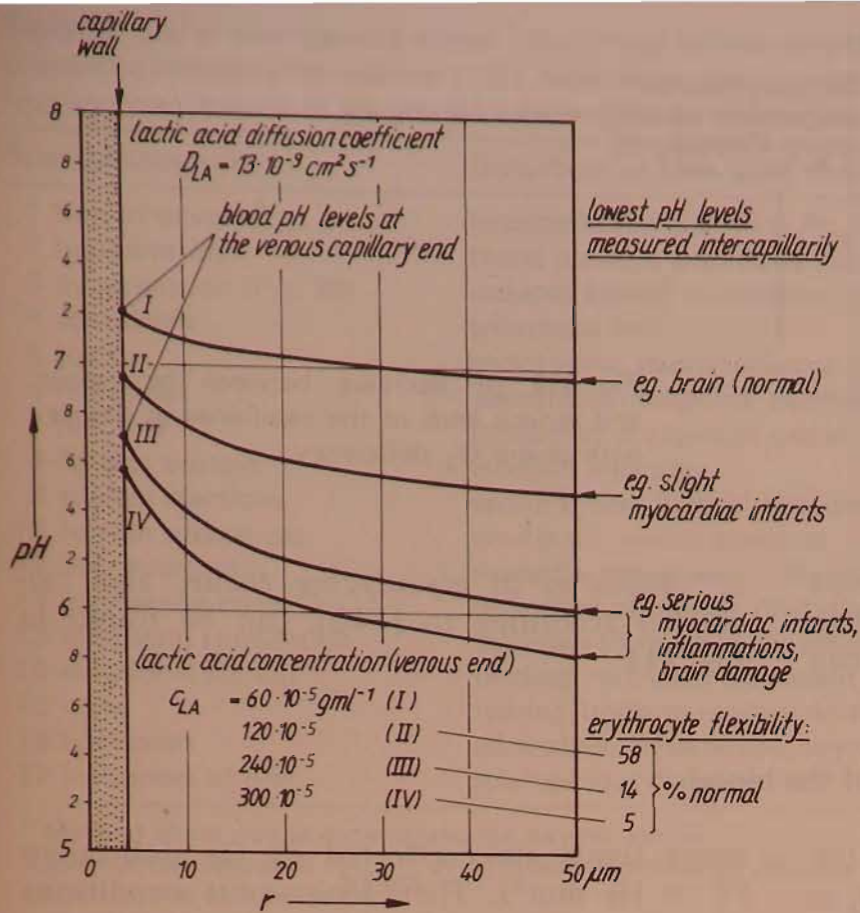


Fig. 110 The pH as function of the distance from the capillary axis r in the venous capillary area of tissue volumes $v \geq 10 \text{ mm}^3$, under glycolysing conditions (lactic acid formation) of different intensity; calculated according to [140]. The lactic acid accumulation occurring in strongly inhibited microcirculation (e.g. case IV) is neglected. It brings about a significant pH reduction in capillary and capillary vicinity

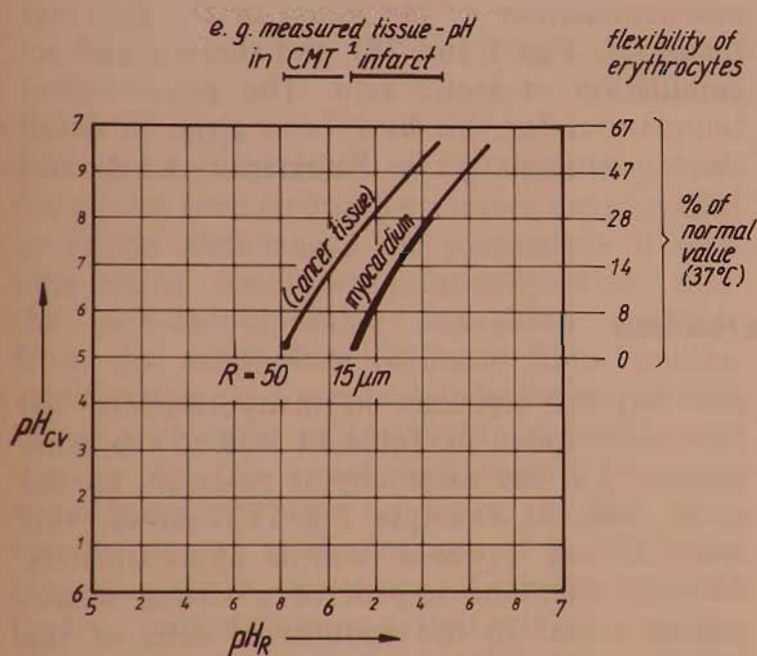


Fig. 111 The pH at the venous end of capillaries (pH_{CV}) in tissues under glycolysing conditions as function of the tissue pH at a given capillary distance R . Approximation according to [140]

¹ CMT = tumor tissue under cancer multistep therapy (CMT) conditions

very small and very large volumes of O_2 deficiency in the myocardium, which are included in Fig. 109. These measurements gave us the pH values for the upper and lower boundary level of the transition curve for normal cells with fermentation metabolism.

According to our model, the following assessment should not be very far from reality: the

lactic acid formation in the space of the narrow glycolytic zone (cf. Fig. 99) of a single intercapillary area is not enough to lead to a considerable reduction of the mean pH level in the interstitium (and at the venous end of the capillary wall). Only when the glycolytic zones of many intercapillary areas come together ($V > 0.2 \text{ mm}^3$) can the reduction of the mean pH in the tissue exceed 0.5 pH units. pH reductions of more than 1 unit in the tissue (and severe pH reductions also at the venous end of the capillary walls), which finally trigger the blood microcirculation inhibition and capillary damage, do not occur until the volume V of the O_2 -deficient area exceeds 10 mm^3 .

The consequences of an O_2 deficit in the various organs and tissues of the human are often determined by the relation presented here. The connection between the size of the volume affected by O_2 deficiency, and the level of the pH reduction which occurs, is thus one of the elementary pathophysiological bases of O_2 deficiency diseases and conditions. It can now be understood why critical consequences (e.g. large-area necrosis after a myocardial infarction, tissue degradation in inflammation processes) only occur when the affected tissue area exceeds a certain volume (e.g. $V \geq 10 \text{ mm}^3$).

pH profiles in the intercapillary space, which can be expected for the venous capillary area of glycolysing tissue regions exceeding the above mentioned minimum volume of 10 mm^3 , as in [140], can be seen in Fig. 110.

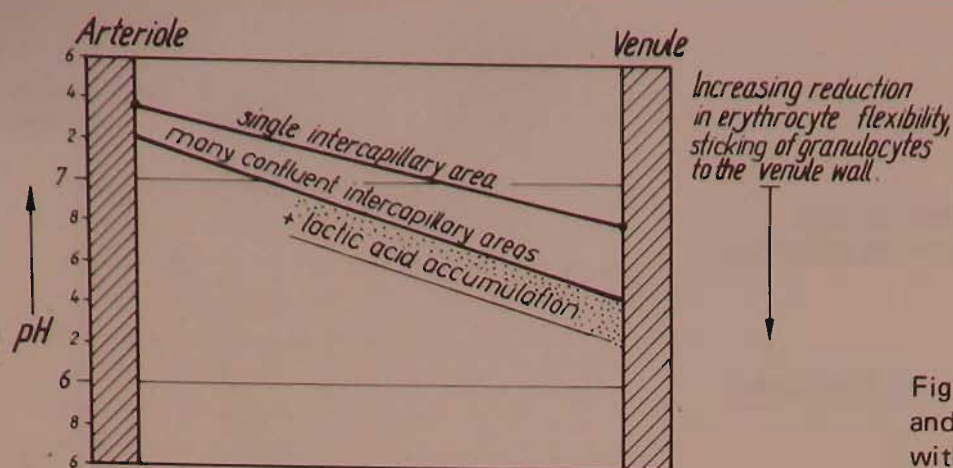


Fig. 112 pH decrease between the arterial and venous ends of the capillaries in tissues with severe O_2 deficiency

An approximation of the connection between the tissue pH measured at a certain capillary distance r , and the pH level at the venous end

of capillaries in glycolyzing tissue, also calculated according to [140], can be found in Fig. 111.

1.4.6 Reduction in the microcirculation of the blood

The lowest pH level in the capillaries of the tissue area with O_2 deficiency always exists, as can be seen from Figs 110 and 112, at their venous end, where the lactic acid formed by glycolysis in the intercapillary space flows away [140]. A further reduction of this lowered level, roughly over the whole length of the capillaries, occurs, according to the preceding paragraph, in

larger tissue areas affected by O_2 deficiency ($V = 10 \text{ mm}^3$). Then there exist conditions which result in a *drastic deterioration in the microcirculation of the blood in O_2 deficient tissue* (cf. Figs 1 and 75), and thereby and accumulation of lactic acid. The physiological foundations for this have been given in detail above, particularly in Paragraphs 1.1.1 and 1.2.1.

1.4.7 Triggering of the non-specific mesenchyme reaction

O_2 deficiency is one of the *sclerogenous noxae* which trigger the *non-specific mesenchyme reaction* discovered and described by Hauss [172, 194]. It can even be ascertained from our investigations (Paragraph 1.1.8.2) that most of the *sclerogenous noxae* in Table 11 cause O_2 deficiency (example Fig. 34) or contribute to it. The mesenchyme reaction must therefore be added to the consequences of O_2 deficiency in the organism which often intrude deep into human life, as it instigates the process of arteriosclerosis, which has serious consequences, and, according to speculative ideas, the reaction could also be involved in the emergence of *alterations in the lung function parameters after noxae and physical exertion, or O_2 MT in the framework of the cellular vessel wall switching mechanism* (swelling of the capillary endothelial cells in O_2 deficiency, Fig. 2).

The reactivity of the cells included under the notion of mesenchyme cells (e.g. *endothelial cells of the vascular intima*, fibroblasts, fibrocytes, *pericytes*, smooth muscle cells of the vascular media etc.) exceeds that of all other

cells of our organism in many respects. All factors compiled in Table 11 lead to the same process, i.e. the mesenchyme reaction. In the aorta wall, as example Fig. 113 shows, this reaction can proceed within approximately 90 min after the impact of a strong sclerogenous noxa. In the endothelial cells of the capillaries (smaller volume involved), the reaction rate should be near to 10 min according to our findings with the 15 min O_2 MT quick procedure. The incorporation of the mesenchyme, e.g. into the aorta wall, is followed by the incorporation of lipids, but only after a delay of approximately 6 h. The extent of the triggered incorporation of the mesenchyme into the vessel wall, and the quantity of the initially gradually gathering deposition products, depend on the strength and duration of the sclerogenous irritation. Thus these determine whether or not the occurring change in structure should be deemed as pathologic.

The structural changes in the vessel wall usually regress after the sclerogenous influence has faded away (reversible phase). If, however, the

Table 11 List of sclerogenous noxae.¹ Disturbing factors which, according to W.H. Hauss, regularly trigger the unspecific mesenchyme reaction [172], detected by the increased rate of ³⁵S-sulfate incorporation into the sulfo-mucopolysaccharides of the ground substance of connective tissue in various organs (animal experiments)

Sclerogenous noxa	Disturbing factors
1 lack of oxygen ²	hypobaric chamber with P_{O_2} values < 150 mmHg
2 hypotension	blood pressure amplitude too low (e.g. < 25 mmHg)
3 hypertension (Fig. 39)	reduced kidney circulation; hypertension (systol. blood pressure > 200 mmHg)
4 operations	anesthesia etc.
5 toxins	endotoxins, staphylococcus toxin, diphtheria toxin
6 infections	pasteurella multocida, staphylococci
7 nicotine	inhalation of cigarette smoke
8 foreign protein	albumin injection
9 allergic reactions	serum shock, Arthus' phenomenon
10 foreign substances	croton oil, plastic products
11 over-exertion	excessive movement in the treadmill
12 mechanical stress	laceration of muscle, dilatation of the aorta
13 interbrain stimulation	thalamus stimulation by means of electric current
14 emotional stimuli	binding, restricted movement
15 noise	roaring, uniform random noise
16 hormones	adrenaline, testosterone, thyroxine, cortisone, glucagon
17 influences of diet	sclerogenous diets

¹ Most of these noxae deteriorate the oxygen status

² Subnormal values of $P_{O_2\text{-art}}$ or η ; locally reduced O_2 delivery to the vessel wall; mechanical irritation at ramifications in the arterial system

sclerogenous irritation or O_2 deficiency lasts for a long time (reduced clearance capacity due to energy deficiency) and particularly if such long-lasting conditions frequently recur, then the non-decomposable deposition products from the metabolism (collagen fibre bundles, calcification etc.) accumulate in the way shown by the electron micrographs in [172]. The damage to the vessel wall caused by these breakdown products no longer recedes (irreversible phase), as the increase of the diffusion length in both directions of the vessel wall (radial, central) begins definitively to limit the metabolism there. A final stabilization of the hypertrophic structure thus occurs. We therefore believe that the pathological changes in structure of the vessel wall remain reversible for a long time. The important thing is that the arteriosclerosis be combatted in this phase, before the irreversible wall degeneration finally takes place. We have already seen [2, 8, 106] the reversal of the sclerogenous noxa "oxygen deficiency" as a *method of renormalization of the vessel wall structure in the reversible phase*, i.e. the O_2 MT in a highly intensive variant adapted to the part of the body in question.

Strict fasting discussed in Paragraph 5.3.9 (Table 42) should also be mentioned as a further method for the renormalization of arteriosclerotically degenerated walls of arteries

and arterioles, and of degenerated layers of the alveocapillary system of the lung.

According to [172] the pathological changes in the vessel wall structure caused by the non-specific mesenchyme reaction affect mainly arterial vessels and their ramifications. Despite this, this reaction could always result in a deterioration of the O_2 supply to the tissue via capillaries, above a certain intensity. This deterioration should result from the reduction of the blood flow (cross-section narrowing, reduction in vasomotoric adaptability and in the air chamber effect) in sclerotically degenerated arteries.

A related reaction in the fine blood capillaries causes the vessel wall thickening discussed in 1.1.1, and thereby a narrowing of the lumen and even a direct hampering of oxygen and substrate diffusion to the intercapillary space. The *basal membrane thickening of the capillaries* due to protein deposits is a well-known phenomenon in diabetic (micro)angiopathies and kidney diseases. The same process can also occur in the membranes of the myelin sheath (Paragraph 1.4.11) and then leads to the neuropathies of the diabetics. In connection with this we should mention that these pathogenic basal membrane thickenings can be broken down by strict fasting (and also by O_2 MT).

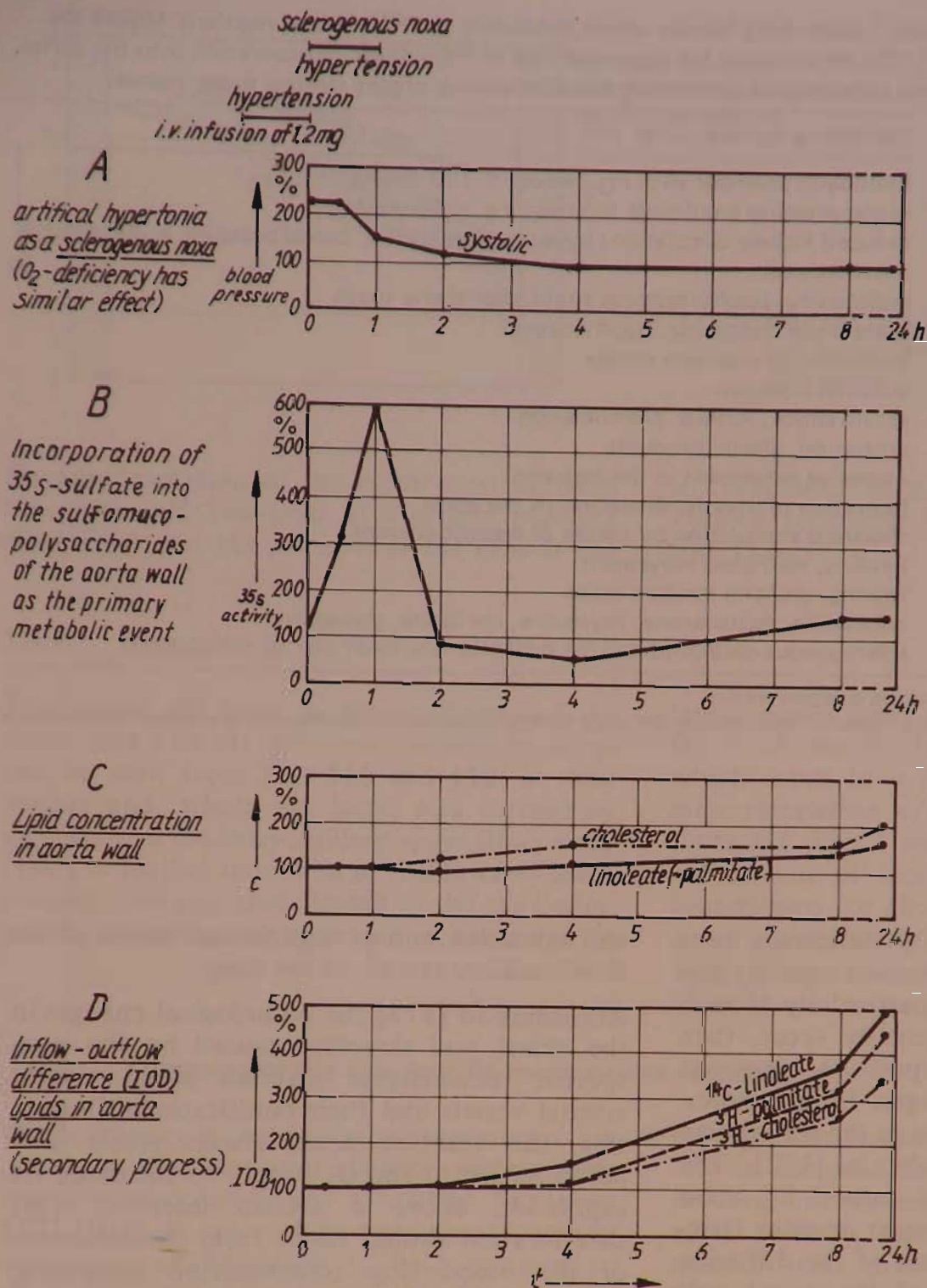


Fig. 113 Measurement on rats to show the fast onset of the unspecific mesenchyme reaction (B) after the raising of a sclerogenous noxa (A). The deposition of lipids into the vessel wall only occurs about 6 hours after the incorporation of mesenchyme (C) (D). Modified according to [172]

¹ A related fast reaction might be the swelling of endothelial cells in capillaries, likewise triggered through O₂ deficiency

1.4.8 Triggering of the formation of lysosomes

The *lysosomes* discovered by De Duve are membrane-delimited cell organelles which fulfil various functions. The primary lysosomes, formed from the endoplasmic reticulum and the Golgi apparatus, contain in a "packaged" form (with great stability against their aggressive contents) a mixture of more than 35 enzymes, mostly hydrolases [195], whose activity

optimum generally lies in the acidic range (pH = 5–6). The enzyme mixture is composed in such a way that it fulfils the following *main functions*:

1. Autolysis of the cell as soon as, on their death, the lysosomal membrane breaks off and the enzymes are intracellularly released;

2. Contribution to the damage to neighbouring or foreign cells, as soon as the enzymes reach the extracellular space as a result of autolysis or exocytosis. Because of the pH dependence of the activity of the decisive enzymes, this contribution is particularly great in over-acidified tissue [2, 141];

3. Digestion of foreign substances, which are taken up by the cell by endocytosis, in the secondary lysosomes, which are formed by the fusion of primary lysosomes with the foreign substance entrapped in intracellular vacuoles;

4. Digestion of the cell's own waste products in the secondary lysosomes.

Functions 1 and 2 are of particular interest in the framework of the theme of this book. It is odd that very little space has hitherto been accorded to these two functions in the greatly expanding lysosome literature [195].

The lysosome content of the cells and the spectrum of the enzymes contained in the lysosomes vary greatly according to cell type [196]. But even for a given cell type, the mean lysosome content is not a constant value but, as the following comparison shows, a value which can depend on the situation of the cell in the intercapillary space: it is known that heart muscle cells in the healthy myocardium contain few or no lysosomes. The electron micrograph, in Fig. 114, of a healthy, well-supplied heart muscle should be looked at here [81]. There is a very high lysosome content in the myocardial cells of the hypertrophic heart muscle, however. The electron micrograph in Fig. 115 proves this, as it shows a very high density of lysosomes [197]. From the theory of substrate diffusion in the intercapillary space of the myocardium [198] it follows for the case of the hypertrophic heart muscle that the P_{O_2} level sinks to values below 10 mmHg (1.3 kPa) at

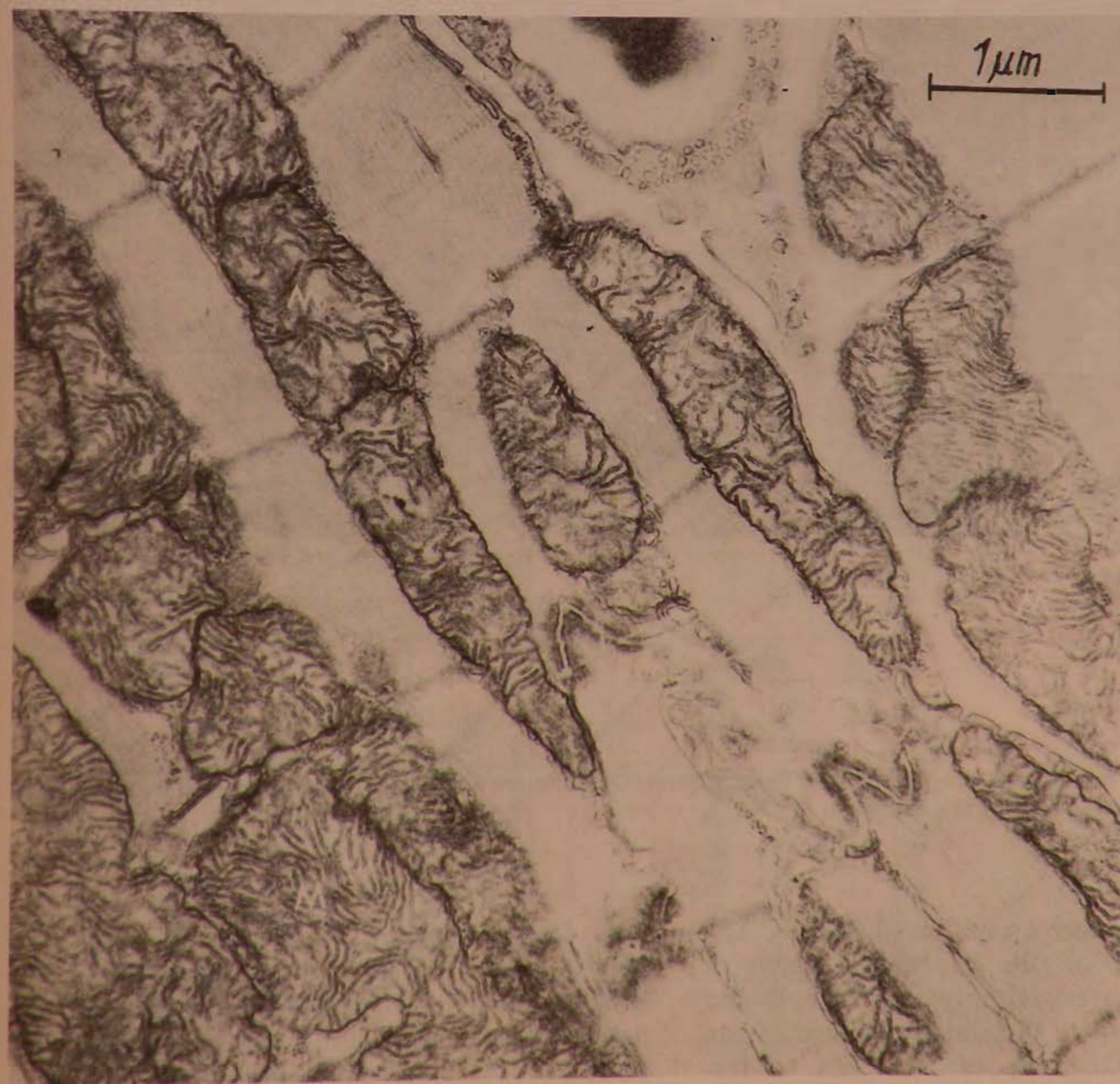


Fig. 114 Electron micrograph of a tissue sample of healthy, well-supplied myocardium; next to the muscle fibers, chains of mitochondria (as also in Fig. 115); no signs of O_2 deficiency, no lysosomes in this section

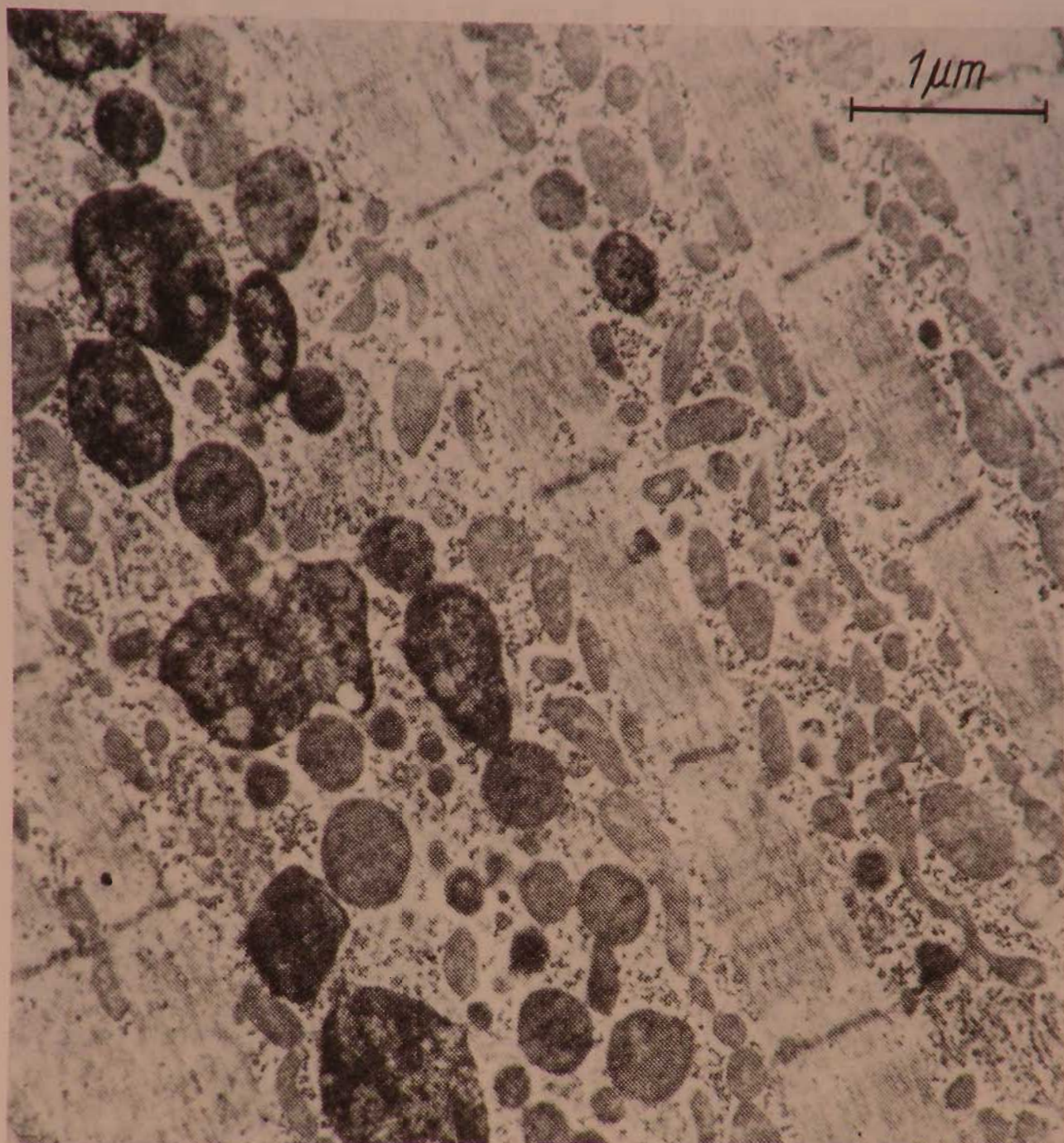


Fig. 115 Electron micrograph of hypertrophic myocardium; O_2 deficiency in parts of the intercapillary space, high density of lysosomes L in this specimen [197]

the site of the greatest capillary distances. The O_2 metabolism of the myocardial cells is thereby unsaturated (supply deficiency), and there finally follows the sudden change of the metabolism of the myocardial cells to fermentation (lactic acid formation) at $PO_2 \approx 3.5$ mmHg (0.46 kPa). *The spontaneous lysosome formation evidently begins as soon as the cell is*

only deficiently supplied with O_2 , and glycolysis looms [199]. This should be seen as a process occurring in the living organism which deserves great attention due to its probably universal character.

By lysosome formation and by the sudden change to fermentation metabolism with a strong pH reduction as a result, Nature seems

to be preparing for the dissolution (digestion) of the cell material, when cell death becomes apparent as a result of a longer duration of O_2 deficit. If larger cell complexes are drawn into the deficiency situation (cf. Fig. 109) then, according to Paragraph 1.4.5, the reduction can

reach levels near $pH = 6.0-6.3$, at which the membranes of the lysosomes become permeable, the lysosomal enzymes are released, and at which, furthermore, a strong activation of the pH dependent enzymes occurs. The final stage is the dissolution of the cells (necrosis).

1.4.9 Triggering of the lysosomal cytolysis and cytolytic chain reaction

Lysosomal autocytolysis. The death of cells is connected to several as yet unsolved problems. The occurrence of cell death can be defined as the timepoint at which the outer cell membrane delimiting the intracellular space becomes irreversibly permeable and the cell interior thereby becomes stainable (e.g. trypan blue test [2]. The activity of the hydrolytic enzymes existing in a single cell (and stored there initially in the lysosomes) is usually enough, after intracellular release and a certain reaction time in O_2 deficiency, to damage the outer cell membrane irreversibly, even at almost neutral cellular pH, i.e. to kill the cell. Autocytolysis does not occur, however, as experiments show, if the outer noxae (e.g. extreme O_2 deficiency, overacidification, hyperthermia) cease soon after the intracellular release of enzymes, as is shown in Fig. 116, left. In such a case, the released lysosomal enzymes are evidently quickly re-

entrapped in newly-formed lysosomes. Such a compartmentalization demands energy, hence oxygen, for thermodynamic reasons. Thus, in this aspect, too, O_2 deficiency should strongly promote autocytolysis. The site where cell decline occurs mainly as a result of autocytolysis can be considered to be the "lethal corner" at the venous end of the intercapillary space. We understand this, for example, for the elementary process of the ageing organism's adaption to the drop in the O_2 supply capacity in older age.

Lysosomal cytolytic chain reaction. We define the lysosomal cytolytic chain reaction [2] as a mechanism of cell damage, by which lysosomal enzymes entering the extracellular space from a dying cell contribute to the death of neighboring cells. The extracellular appearance of the enzymes only occurs (Fig. 116) after a certain

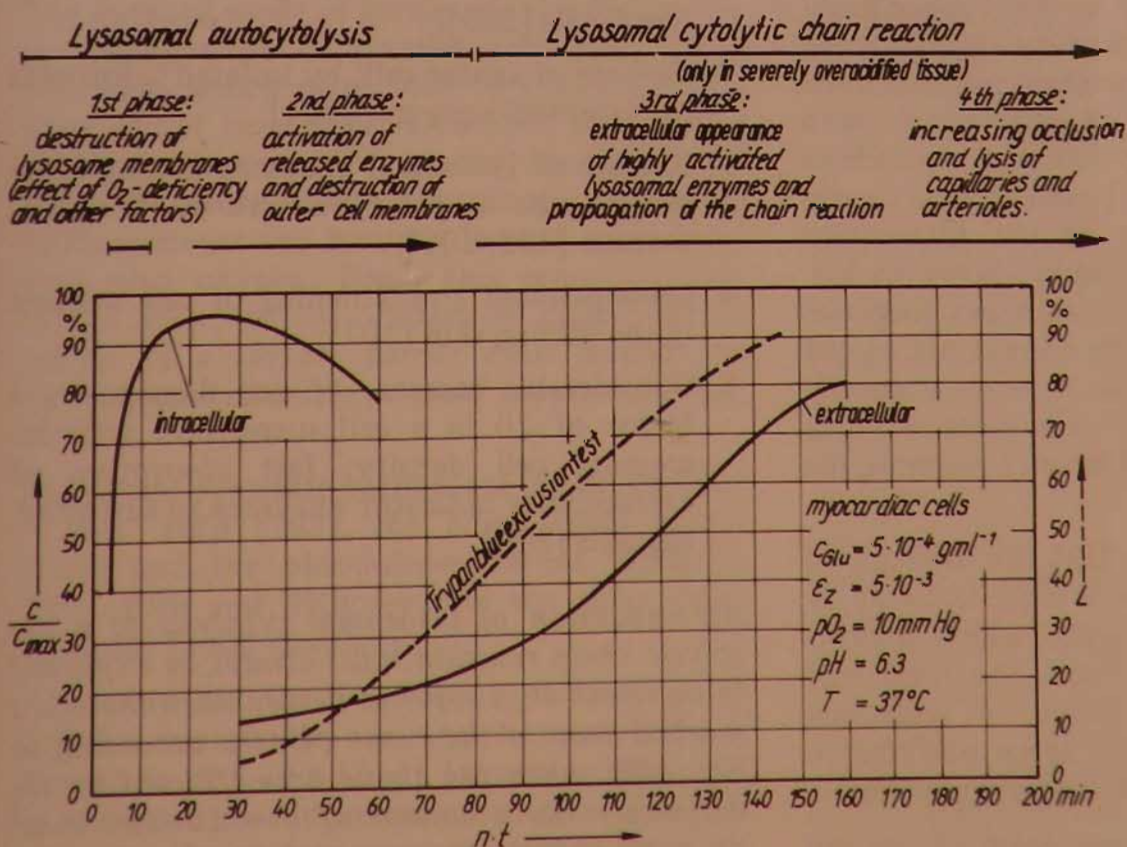


Fig. 116 Guiding values for the relative concentration c/c_{max} of lysosomal enzymes in the intracellular and extracellular space of model cells, as a function of the reaction time of $pH = 6.0$ in vitro. Extrapolation according to measurements on EMAC [2] and myocardial cells [146]. n = factor near 1, dependent on the matrix and the content of lysosomes in the respective type

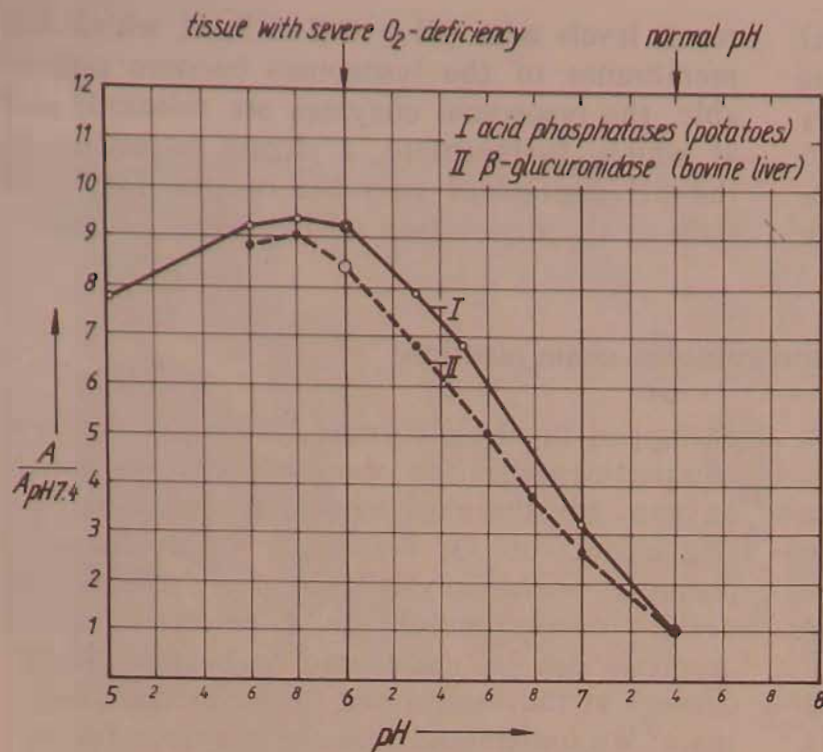


Fig. 117 Increasing activity of two lysosomal enzymes (examples) at $T = 37^{\circ}\text{C}$ in the transition from normal pH in healthy tissue to the mean pH of tissue with severe O_2 deficiency [141]

time span (autocytolysis time, e.g. 120 min). The cytolytic chain reaction is thus a slow process lasting many hours (e.g. 4–23 h, according to number of reaction steps and conditions). In connection with this we should think of the acute phase of the myocardial infarction [200], which occurs in roughly such time spans, for which we assume a lysosomal cytolytic chain reaction [2, 144, 171].

The cell-damaging chain reaction can only reach great intensity in highly overacidified tissue, and even there remains in its “subcritical” range, i.e. it will only have effect-strengthening properties. That a cytolytic chain reaction must occur in highly overacidified tissue can be seen from the pH activation of the lysosomes already described in [201], and just as clearly from the typical courses of the pH/activity curves of lysosomal hydrolases shown in Fig. 117. The activity of such enzymes increases nearly tenfold between the normal pH of the tissue and a pH level ≈ 6.0 . A severely damaging effect on the adjacent cells must result in the acidic milieu of such enzymes reaching the extracellular space.

Added to this is the fact that the drainage of these enzymes is made much more difficult by the inhibited microcirculation which prevails in severely overacidified tissue. This must lead to an increased concentration of lysosomal enzymes in the intercapillary space, and thus to a further strengthening of the chain reaction.

The stop in O_2 supply when death occurs can be regarded as a border case of O_2 deficiency, both as regards its intensity and its spatial extension. As suggested in the presentation in Fig. 118, lysosomal cytolysis and cytolytic chain reactions are evidently also effective in the

living organism, in order to initiate its general disintegration immediately after death [202].

The lysosomal cytolytic chain reaction has been the object of several investigations carried out since 1965, which are summarized comprehensively in [2, 141, 171]. In a series of in vitro and in vivo experiments, *experimental indices for the in vivo existence of the cytolytic chain reaction in highly overacidified tissue* were found:

1. Damage of cancer cells by addition of cytolysed cells [203];
2. Damage of cancer cells by isolated lysosomes or lysosomal enzymes [204];
3. Release of lysosomal enzymes in and from cancer cells at $\text{pH} = 6.2$ and 40°C hyperthermia [205, 206];
4. pH-dependent strengthening of cell damage in the human skin [207];
5. Considerable increase of cell damage by a factor of 20 in a cell suspension with increasing cell density; fast adsorption of extracellular indicator enzymes to surrounding cells [208].

An expansion of lysosomal cytolysis to a cytolytic chain reaction must always be expected in deficient O_2 supply in tissue, when there is a marked drop in the tissue pH, i.e. according to Fig. 109, when the tissue area affected by O_2 deficiency has a volume of $V \approx 10\text{--}100\text{ mm}^3$ or more (examples: myocardial infarction, inflammation). The chain reaction proceeds up to the geometrical limit of the overacidification, and there ceases when it reaches sufficiently supplied tissue, particularly when it reaches larger blood vessels.

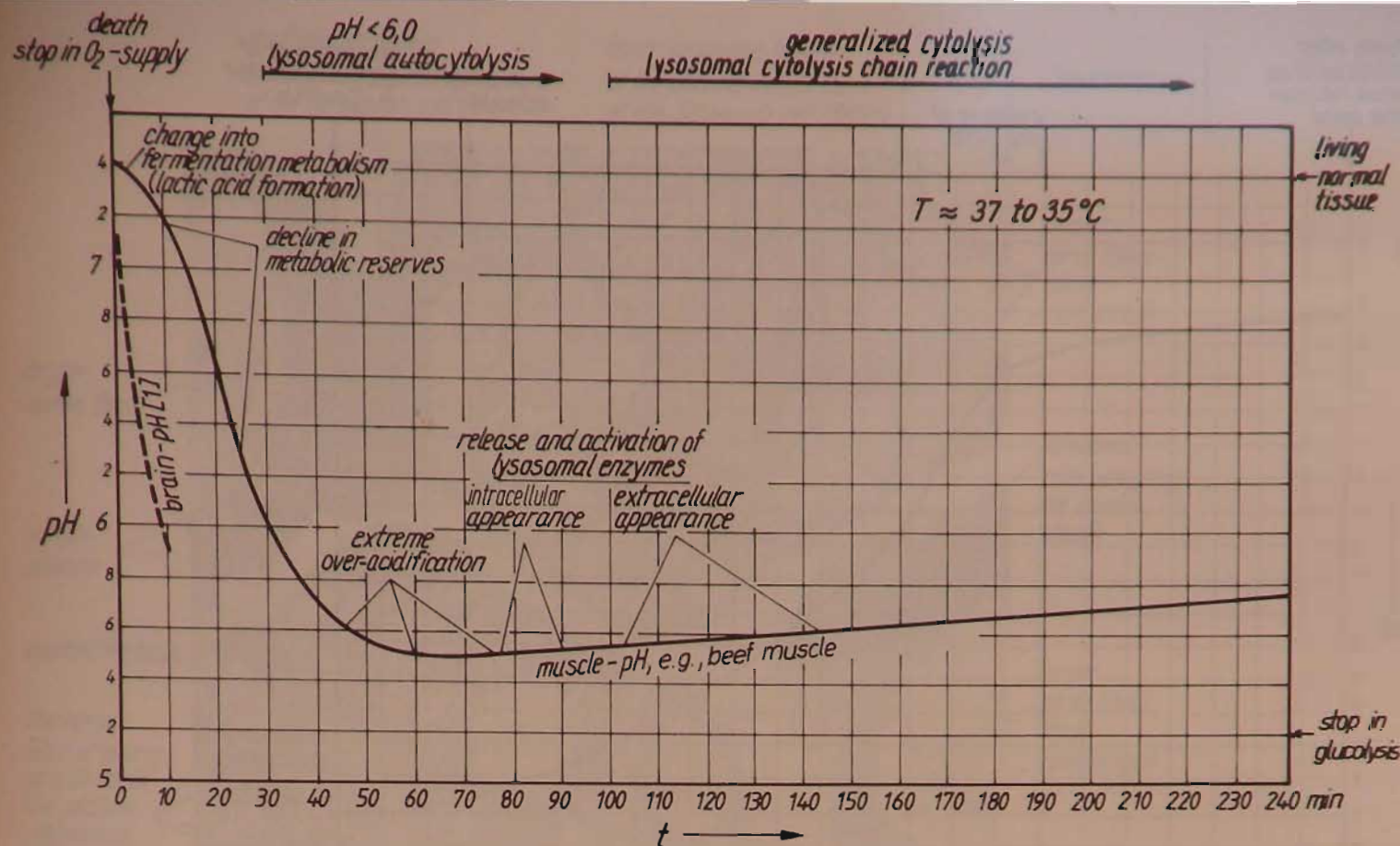


Fig. 118 The pH-controlled basic process of the generalized cytolysis after death occurring at time point $t = 0$

1.4.10 Labilization and stabilization of substrate barriers. Blood-brain barrier and blood-nerve barrier

The detailed mode of action and the damage to, or degeneration of metabolic barriers in the organism, which often lead to severe diseases, have as yet been little researched. It is certain that the maintenance of the structures and processes which build up metabolic thresholds, compartments and barriers, require energy, and thus also oxygen. From this generally theoretical view, *an O_2 utilization deficit in the region of a certain barrier must labilize the barrier and inversely, a good supply must stabilize it.*

Important substrate barriers are the blood-brain barrier, BBB [192], the blood-liquor barrier [209] and the blood-nerve barrier, BNB [2, 210]. BBB and BNB separate the nerve tissue from the blood circulation.

The contribution of aerobic glycolysis of the glucose metabolism in the human brain is known to be 8–9% [211]. Largely independent of the glucose concentration in the blood circulation, the glucose concentration in the brain tissue is kept at approximately 6 mg/100 ml [212] and the acidification of the brain tissue at $pH \approx 7.05$ [215] due to the existence of the BBB. If the BBB collapses (e.g. death caused by

anesthesia, death in diabetic coma), a very fast drop in the cerebral pH to levels of around 6 occurs, and, followed a few minutes later by death. A pH recording in the cerebral cortex in artificially induced hyperglycemic coma is shown and commented on in Fig. 119. In the framework of research for the development of the cancer multistep therapy [2, 22, 23, 125], where the blood glucose concentration is set long-term at up to $8 \cdot 10^{-3}$ g/ml (800 mg/100 ml), a labilization of the BBB due to narcosis is strictly avoided, and a *stabilization of the BBB and of the blood microcirculation in its vicinity by means of the O_2 MT measures is always striven for.* With the resulting good stability of the BBB, the blood glucose concentration can be increased, e.g. for 25 h to 5–6 times its normal level, without particular risk for the patient [214], without considerably more glucose entering the brain, without an increase of aerobic glycolysis there, and without a noticeable increase in the natural, slight acidification of the brain tissue [213]. In the region of a brain tumor, no BBB limits the tumor overacidification of the CMT.

The cells of the peripheral nerve system also

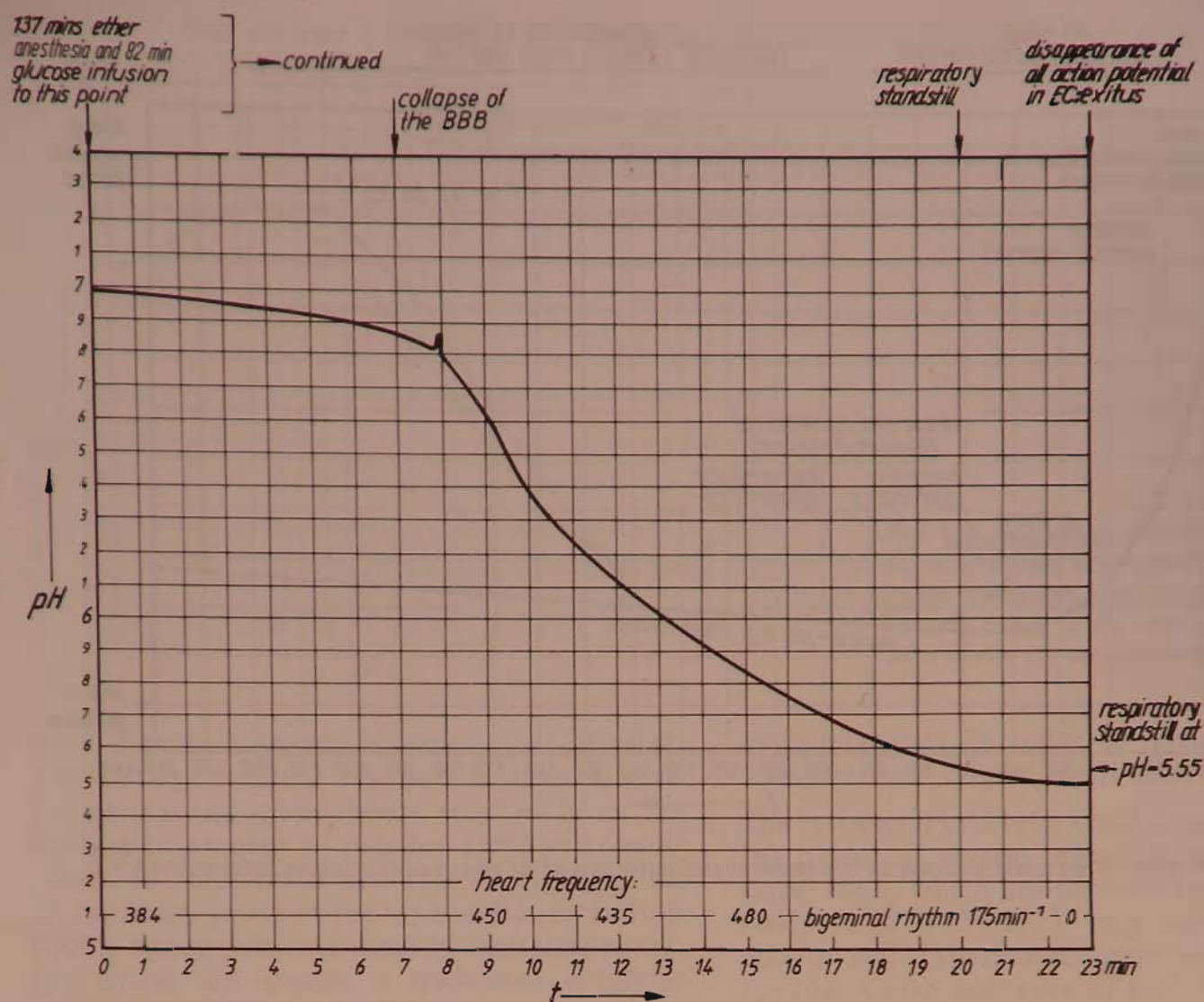


Fig. 119 pH registration in the cerebral cortex of a rat under severe hyperglycemia ending in irreversible hyperglycemic coma. At very high blood glucose concentrations, ether anesthesia contributes to labilization and break-through of the blood-brain barrier

have a considerable aerobic glycolysis, which leads in vivo in the nerve fibres to a pH of approximately 6.8–7 (unexcited state) [215].

The known experiences with diabetics having a temporarily severely increased blood glucose concentration suggest that, for the peripheral nerves too, the glucose concentration must level off to a constant value largely independent of the blood glucose concentration. The existence of a blood-nerve barrier (BNB) [210] which limits the passage of glucose can be seen experimentally in that no nerve pains are observed in such cases. This observation means that, due to the high sensitivity of the nerves to over-acidification [32], no significant reduction of the neural pH occurs.

New results of electron microscopic tissue research show that the structure of the BNB is mainly represented either by a multi-layered

cover of the nerve fibres (myelin sheath of the larger fibres) or by an oligo-layered coat on the plasma membrane of the Schwann cells. These structures can be clearly seen on the electron micrograph in Fig. 120 from [81].

In connection with this we should refer to the outdated formulation [32, p. 5] on the significance of the myelin sheaths or glia cells: "It is unclear whether the glia cells play a role in the metabolism of neurons." The knowledge of the existence of the BNB should lead to new aspects in the explanation and therapy of various complaints and diseases of the peripheral nervous system (action of certain nerve toxins, atrophy of the myelin sheaths, diabetic neuropathies with swelling of the basal membranes, partial pareses, multiple sclerosis, neuralgia etc.).

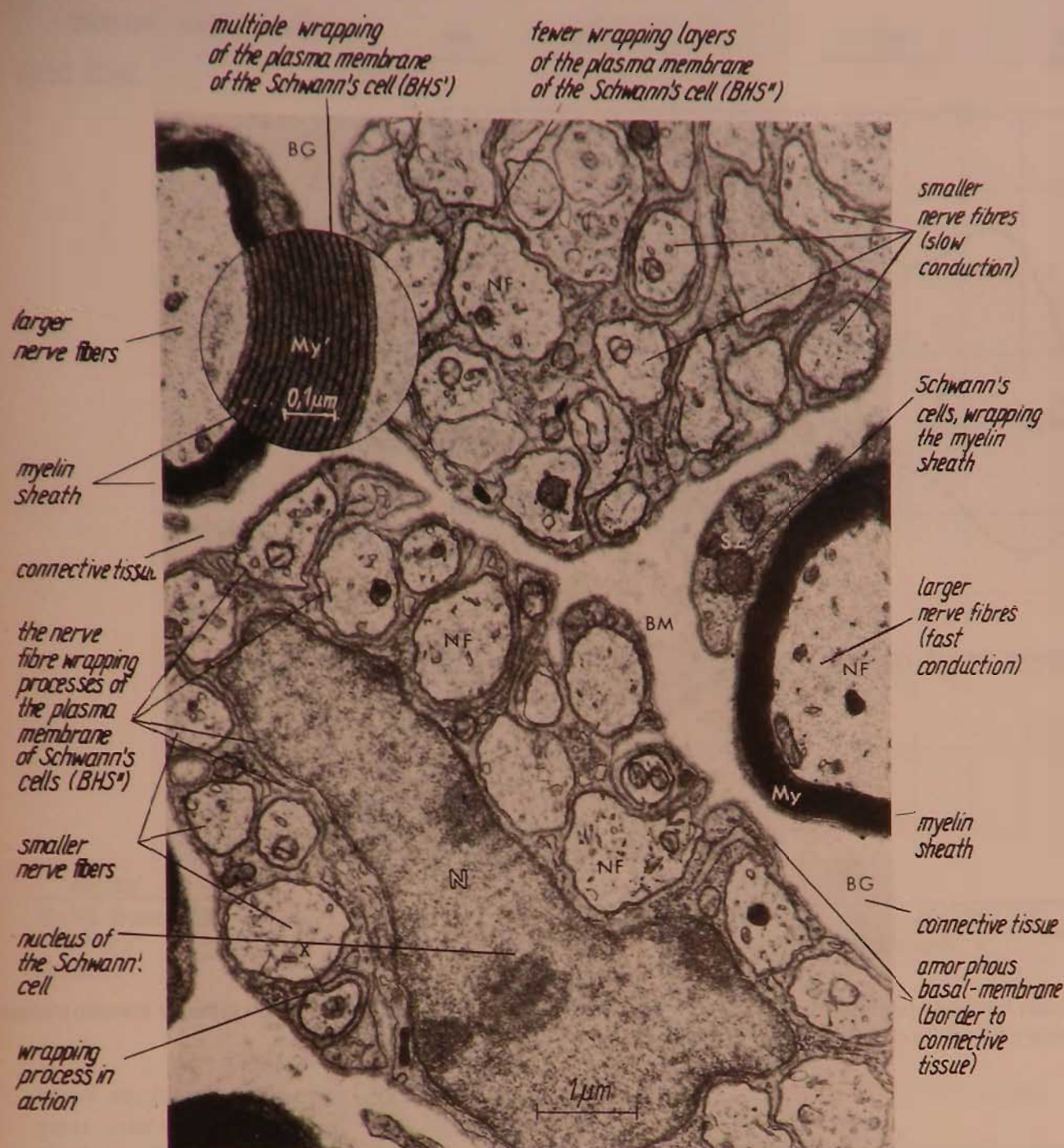


Fig. 120 The blood-nerve barrier (BNB) in the electron microscopic picture¹. The discovered BNB [210] limits the traverse of glucose to the peripheral nerves and causes the amount to be virtually independent of the glucose concentration in the blood circulation. In this way the BNB keeps the proportion of aerobic glycolysis of the nerve cells constant, and at a level that leads to a pH value that is somewhat lower than in normal tissue, and is necessary for the nerve function (pH $\approx$ 6.8; unexcited condition). The wrapping of the nerve fibres therefore in no way serves isolation alone

¹ Object: skin of laboratory mouse

1.4.11 Pain and blood-nerve barrier

The extreme overacidification of the nerves occurring after injury to the BNB (multiplied glucose offer to the nerve cells with normally only a 9% glycolysis contribution to metabolism; reduction of the pH from approximately 7.0–6.0) can be seen as representing the main contribution to the primary process in the triggering of pain stimuli. It follows from this that the strength of sensation of pain and the level

of glucose concentration in the blood circulation correlate with each other, a known experimental observation in diabetics.

It can be concluded from the similarity of the glucose offer through the blood circulation and from the identity of the metabolic behavior of the cells of the peripheral nerve system and of the brain cells that a pH course similar to that

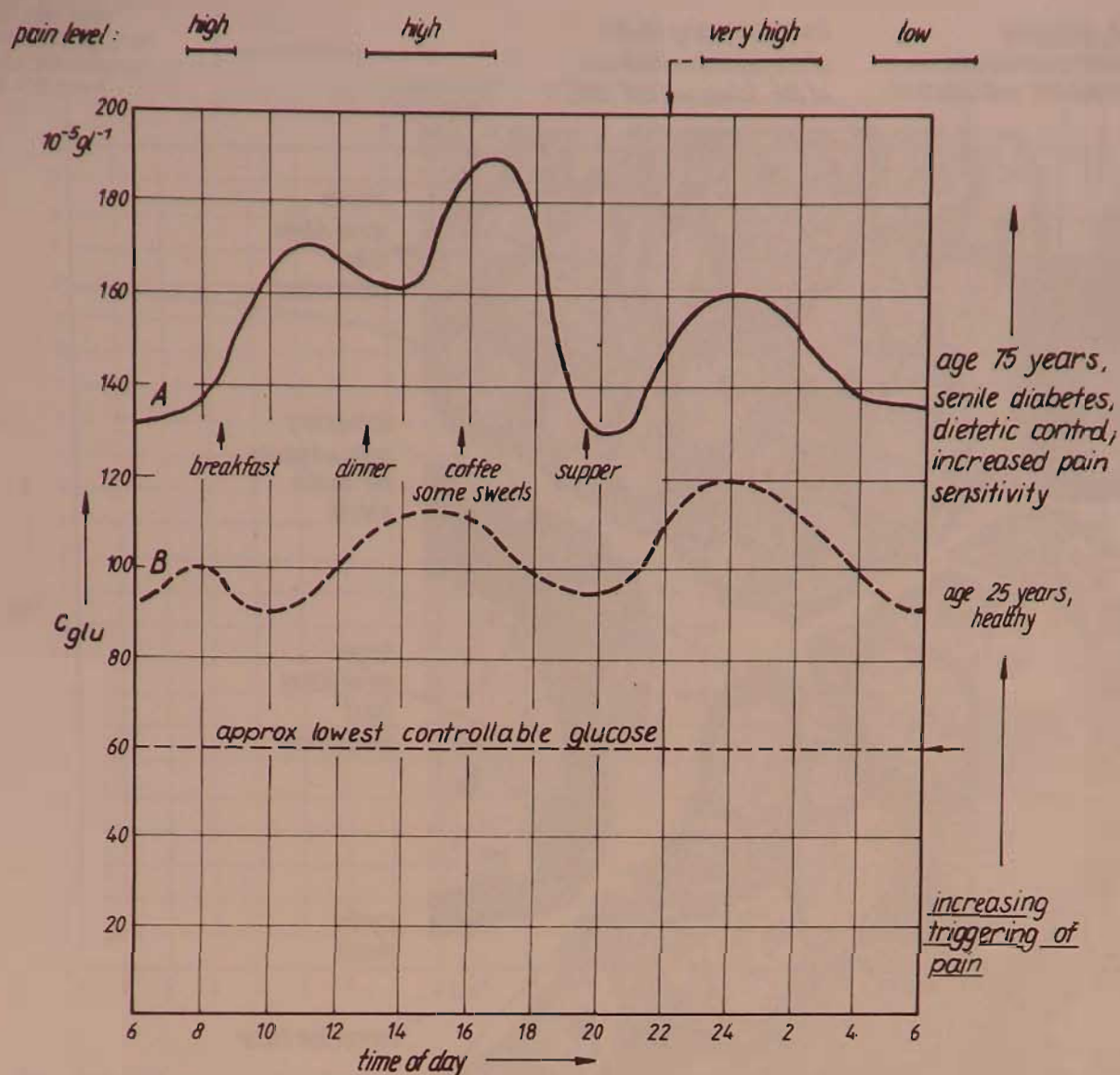


Fig. 121 Correlation between pain and blood glucose concentration. Typical course of blood glucose concentration in the 24-hour cycle of a senile diabetic (A) and a healthy person (B)

in Fig. 119 occurs when the BNB is breached. The overacidification of the nerve fibres then leads to the strong sensation of pain. In this it is, in principle, of little importance whether the damage to the myelin sheath occurs by injuries, by mechanical pressure, by the unrestrained growth of a tumor, or by some other means. Depending on the momentary blood glucose level and the extent of the injury, the damage leads to an increased traversing of glucose to the nerve fiber (this increase is sometimes more, sometimes less, but always great), and thereby to the pH reduction and triggering of pain. When the damage is very extensive (e.g. cancer in its advanced stage, burns etc.), very great pH reductions are to be expected, and particularly severe pain does indeed occur.

It is well known that the blood glucose concentration fluctuates considerably in the 24-h cycle. The typical courses of these fluctuations when the food intake is spread over 4 meals are shown in Fig. 121. Particularly strong fluctuations occur in diabetics (solid line). According

to the discussed ideas about generation of pain, every type should exhibit a corresponding circadian profile with highs and lows. We questioned numerous patients with chronic pain. The result (Fig. 121, above) confirms, in accordance with our hypothesis, that pain sensation is also subject to very great fluctuations in the circadian cycle and that, in good approximation, the pain maxima and minima correspond to the blood glucose profile. Because of the drop in glucose concentration in the nerve tissue as a result of the occurring fermentation, a not inconsiderable drop in concentration to the blood circulation must be assumed for the pain-free condition, in the case of damage of the BNB, too. We estimate that, for moderate BNB injuries, a blood glucose concentration of approximately $40-60 \cdot 10^{-5} \text{ g/l}$ for freedom of pain must be allowed for. Further research should be undertaken for the accurate, quantitative determination of this blood glucose threshold level of freedom from pain and its variation, dependent on the extent of the BNB damage, a level which

Glucose concentration in:
nerve tissue

Remarks

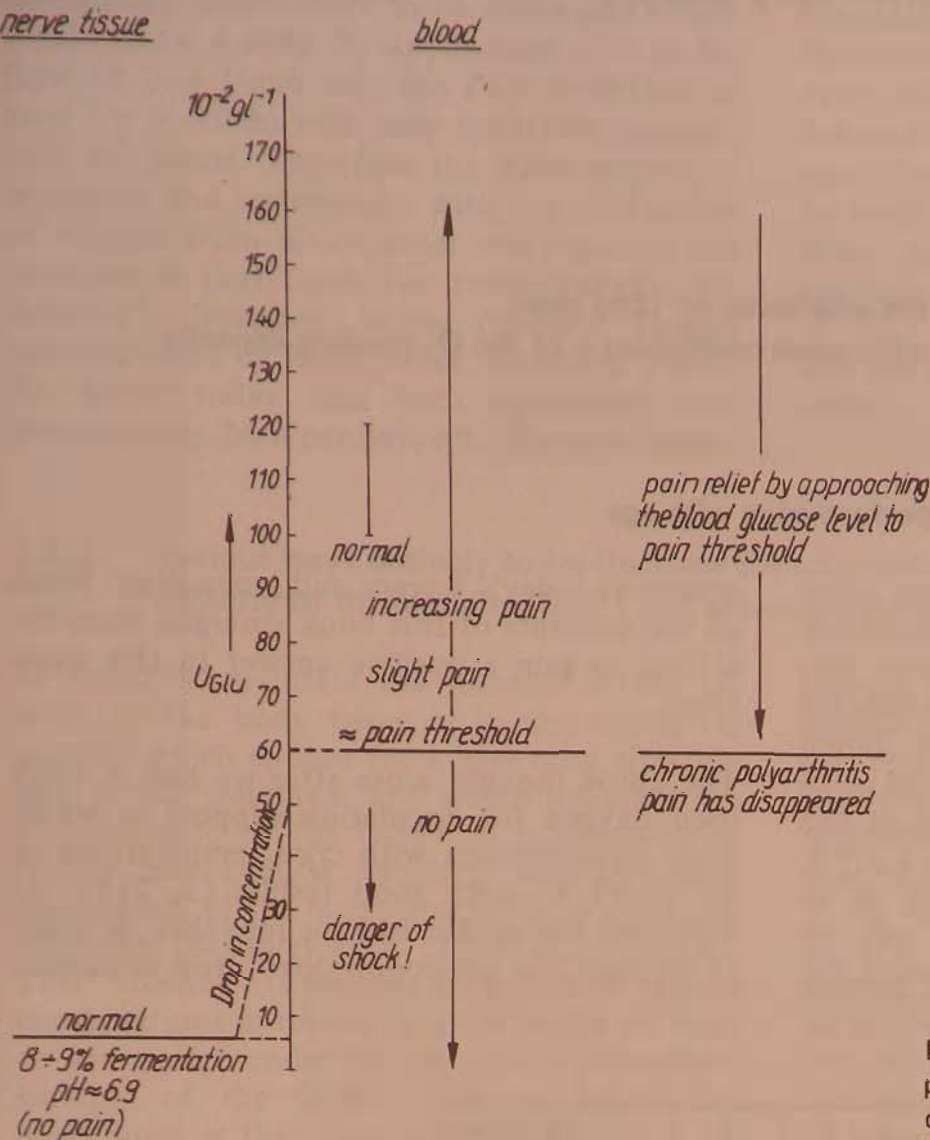


Fig. 122 Relief of physical pain by approaching the blood glucose level to the observed "pain threshold"

is of such importance for pain theory. To support our estimation we include a finding of Caspers (Deutsches Zentrum für Sauerstoff-Mehrschritt-Therapie, Bad Füssing, FRG), on the *complete disappearance of very severe polyarthritic pains when the blood glucose level was reduced to $60 \cdot 10^{-5}$ g/l.*

The above considerations lead to a *basic recognition of the combat of physical pain by reducing the blood glucose*: the pain does not disappear only when a zero blood glucose level is reached, which could never be attained due to the known reasons of hypoglycemic shock, but much sooner, by reduction to levels of around $40-60 \cdot 10^{-5}$ g/l. Thus there exists a *pain threshold of blood glucose concentration.*

The finding of the pain threshold means that we must try to come as close as possible to this threshold in the combat of pain, by means of the manipulated (and monitored!) reduction in the blood glucose. Since this threshold exists and, furthermore at glucose levels which are still more or less tolerable, it seems that our path to the combat of pain can be practically

trodden. The overview in Fig. 122 summarizes the above findings.

The further guidelines which follow result from our ideas on the combat of chronic pain: on principle, the aim of all measures must be to *reduce the blood glucose to a level which is as low and as undeviating as possible. The eating of sweets must be cut to a minimum.* In order to reduce the deviations (Fig. 121) we recommend that the normal rules for diabetics be strictly observed, such as adherence to the *diet regulations* to keep the blood glucose at a low level, and the *distributions of food intake over a larger number of meals.*

It is to be expected from the energetic consideration at the beginning of this paragraph that a longer lasting O_2 utilization deficit in the area of BBB and BNB has particularly severe pathological consequences and that, inversely, the measures of the O_2 MT can also help significantly in these fields. However, more than expectation and motivated hope should not be seen in these words, as medical research here is still in its early infancy.

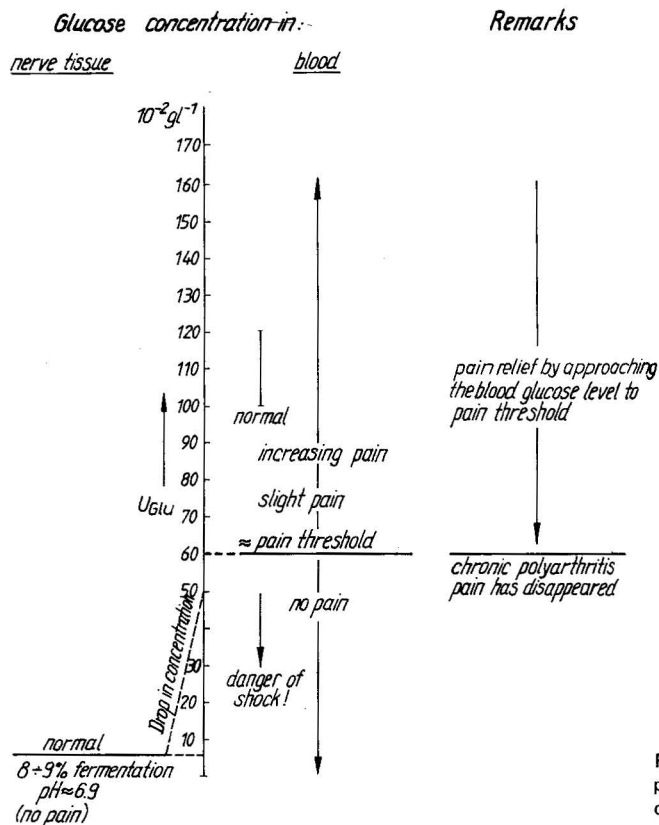


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2. Basis of the main therapy steps

2.1 Increase in the O_2 content of the inhalation air (2nd step)

Ways lastingly to improve the utilization coefficient η of the O_2 -binding capacity of the blood

2.1.1 Reduction in cardiopulmonary performance with age

One physiological "rule" that hung over every human life until 1977 is the *severe reduction in lung performance or in cardiopulmonary performance of the adult organism with advancing age*, portrayed in Fig. 123. This rule should always have been placed at the beginning of all textbooks on geriatrics. The knowledge of this "rule", which was discussed in detail in 1.1.9.5, led us around 1970 to the question as to whether this drop in performance can be temporarily compensated or delayed using the

means of today's science and technology. Much of the contents of this book emerged from the efforts to gain a positive answer to this question.

The above thought arose after we had in 1969 used oxygen for circulation support in whole body hyperthermia with core temperatures of up to 41°C , with good results [2, 218]. At that time the author had the idea that, in order to balance the age-conditioned drop in cardio-

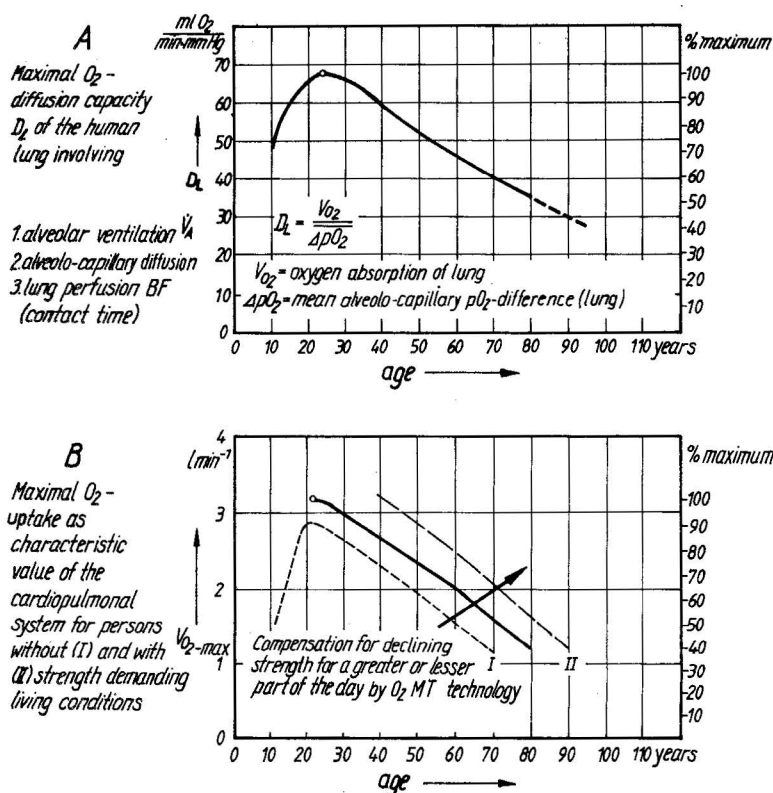


Fig. 123 Maximal O_2 diffusion capacity of the human lung (A) [216], and capacity of the cardiopulmonary system (B) [217] as function of age. In B, the age-dependent decrease of HMV, described in Fig. 67B, is considered

- 1 Environmental conditions of a modern industrialized state
- 2 Favorable constitution, acquired in particular through exercise training

pulmonal performance (see also [219, 220])¹, technology would have to be developed which would allow a daily O₂ application with an O₂ flow of 2–4 l/min over the 24-h cycle (but at least for 8–10 h) with only moderate expenditure of means. Therefore the development of processes and instruments with the production of oxygen from air or water was begun in our Institute at that time. The result was the “O₂ Selector” described below (modern version manufactured by Hauniwerke, Hamburg, FRG). We know today that such equipment used permanently 24 h per day, e.g. in severe chroni-

cally obstructive lung diseases, can increase life expectancy by approximately 7 years [100]. However, we surprisingly discovered [3, 7] that, *even without permanent O₂ application*, the reduced cardiopulmonal performance in old age can often be increased for months up to years to levels existing in youth, if, by means of the three main steps of the O₂MT, the cellular capillary wall switching mechanism described in 1.1.1 has been triggered in the whole body and has led to the lasting distension of all capillaries.

2.1.2 Various ways lastingly to (re-)increase the utilization coefficient η of the O₂-binding capacity of the blood by O₂MT and exercise training

In order to maintain the increase in the O₂ offer to the body tissue or in the resting O₂ uptake, which endure for a long time after the end of the treatment and which represent the characteristic of the O₂MT, it is necessary to trigger the cellular capillary wall switching mechanism of the microcirculation in a positive direction (detumescence of the endothelium). This “steering” is possible by means of various combinations of measures, all of which we want to summarize under the concept of procedural variants of the O₂MT. Common to all the procedures is that they raise the energy or O₂ supply situation above a certain threshold for a certain time. If this threshold is crossed for a certain length of time, then the improvement which occurs in the microcirculation is maintained for a long time.

Typical dosage characteristics of the procedures for the high-charging of the blood microcirculation are compiled in Table 1. The *PO₂ level at the site of the endothelial cells at the venous end of the capillaries* (cf. Figs 3 and 7), and the *circulation volume of the microcirculation* are decisive for the triggering of the switching process. The higher the quantitative values of these parameters, the shorter the treatment time required. A procedure duration of roughly 36 h is necessary in order to attain the O₂MT target, so long as the physical exertion normally obligatory for the O₂MT cannot be performed (non-able-bodied patients) or is carried out between the treatment sessions and the O₂ content in the inhalation mixture is only approximately twice that of the normal level of

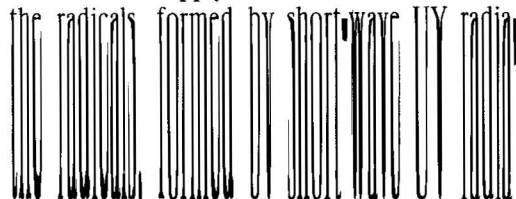
the air, and so long as the normal respiratory minute volume (RMV) is only between 4 (sleeping) and 7 l/min (at rest). If, however, physical exertion of, e.g. 50–100 watt (home trainer) is performed during O₂MT treatment, the RMV rises to levels of between 20 and 33 l/min, and if the volume of inhalation of virtually pure oxygen is aligned with this significantly increased RMV, then *PO₂* levels of an average 60 mmHg (8 kPa) result at the venous capillary end. Since the circulation of the capillaries in the lung and heart area is increased by a factor of approximately 2.3 simultaneously with the increase in cardiac output, a procedure duration of 15 min is then sufficient for the intensification of the microcirculation. The possibility of combining the two procedures just mentioned in O₂MT variants, and ways of designing such variants whose procedure duration lies between 36 h and 15 min, are discussed at a different point in this book.

The findings in [50] show that the method of so-called *hematogeneous oxidation therapy* (HOT* method, ultraviolet irradiation, UVI) according to Wehrli [222], also often intensifies the microcirculation. But this effect frequently fades in the course of a few days, because the efficacy of this method obviously remains close below the switching threshold discussed above (cf. Table 1). Our experiences indicate that the switching effect of the HOT* varies for the different tissue areas of the organism (good effect at the lower extremities). In order to extend the probability of a longer lasting effect for the HOT*, we introduced its combination with procedural variants of the O₂MT [50].

The risk to the patient is minimal in the HOT* method, which works without blood foaming [223]. The risk is higher in the invasive application of ozone [224, 225]. The same catalytic

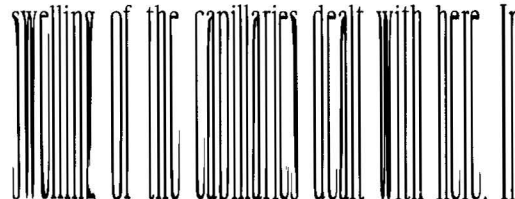
¹ Mean levels of changes in 21 further physiological parameters between the age of 20 and 65 (normal conditions) are compiled in [221]

action of oxygen radicals is to be assumed, and the same limitations and features as with the HOT* should apply. The actual mechanism of



tion, by ozone and also by O_2 activation, as regards the reduction of the endothelial swelling, and the increase in blood fluidity [262], is as yet unexplained. However, what matters is not the explanation, but the effect (which can even be measured here).

Observations made at the capillary wall in diabetic microangiopathy have a certain connection with the reversal of the endothelial



swelling of the capillaries dealt with here. In that case, too, a thickening of the capillary wall occurs, which is, however, attributed to an increase in the thickness of the basal membrane of the capillaries [229–233]. It has not yet been investigated whether this type of thickening can also be reduced by O_2 MT procedures.

2.1.3 PO_2 increase in the inhalation air in high fever and in hyperthermia. Reduction of the rehabilitation time

In high fever, or with high artificial whole body hyperthermia, the O_2 binding curve of the blood is shifted towards the right in its upper part, as seen in Fig. 124. For $PO_{2-art} = 70$ mmHg the O_2 saturation drops by 5.5% from $SO_2 = 93\%$ to 87.5%, when the body core temperature has risen to, e.g. $42^\circ C$. Figure 125 shows an example of the change in the relative characteristic value of the O_2 status (PO_{2-art} ,

PO_{2-art} , η , each at rest) in a flu infection with $40^\circ C$ fever (patient 30 yrs old). The discovered great increase in the resting PO_{2-ven} makes the main contribution to the critical reduction of the η -value to 13%. Roughly the same low levels of η were observed in phases with substantial energy deficit. They are a characteristic feature of conditions of weakness. In such conditions even slight dysfunctions in the cardio-

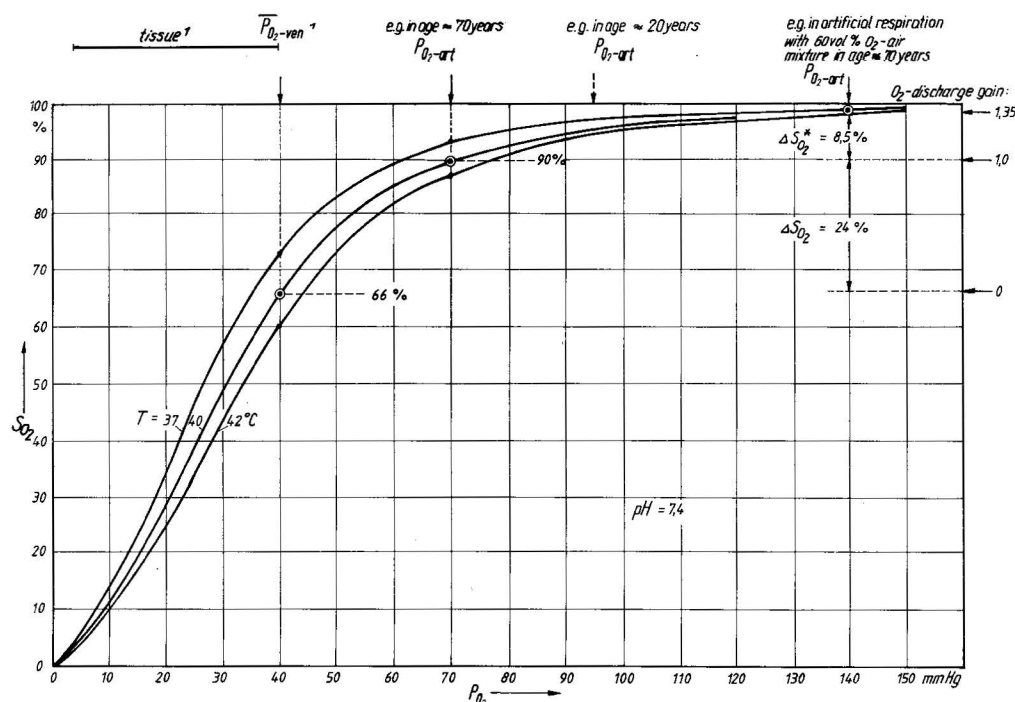


Fig. 124 Curves for O_2 binding in the blood as a function of oxygen partial pressure at 37, 40 and $42^\circ C$. Example of the O_2 discharge gain SO_2 attainable in an elderly person with $40^\circ C$ fever (whole body hyperthermia), when O_2 content of inhalation air is elevated from 20 to 60 vol.-%, in the initial phase of the infection, PO_{2-ven} still remains almost constant

¹ For values in various organs see Fig. 9

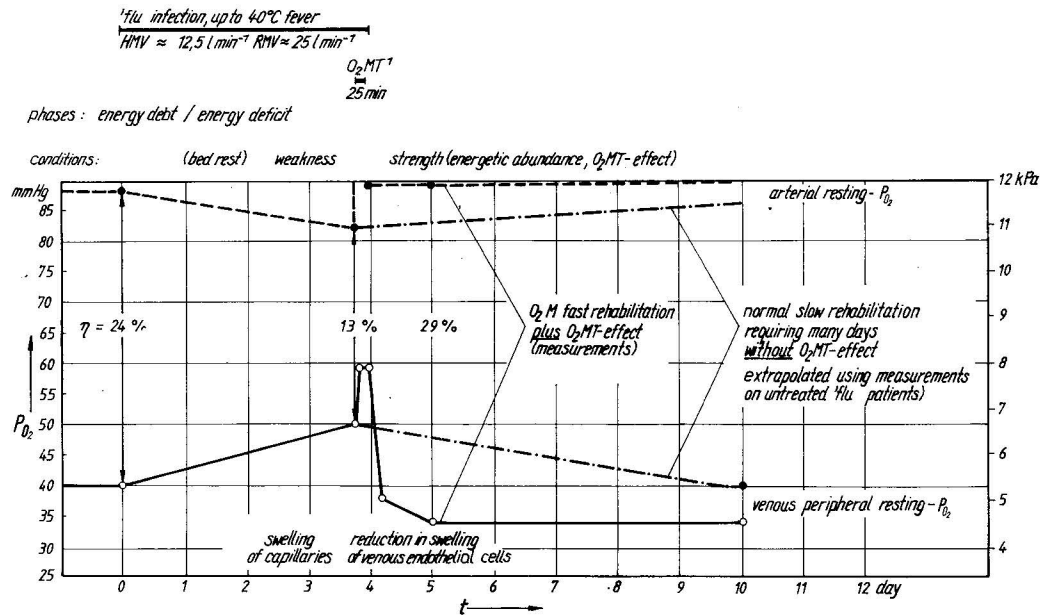


Fig. 125 Example of the course of arterial and venous P_{O_2} (including value of η), under resting conditions, in a 'flu' infection with high fever with and without use of the occurring increase in the heart and respiratory minute volume (HMV and RMV) for an O₂ multistep quick procedure to reduce rehabilitation to a few hours, and to bring about a lasting improvement of the O₂ status. P_{O_2} measurements at roughly the same time of day. Age: 30 years

¹ Mask applicator with storage balloon: O₂ flow 25 l min⁻¹; Oxygenabund 30 min before start of O₂ inhalation

pulmonal system or small increases in strain are enough to trigger circulatory disorders. The application of O₂ is therefore a very helpful measure as a prophylaxis against circulatory disorders in high fever (e.g. attacks of malaria, elevated temperatures accompanying tumor necrosis, sudden attacks of fever in malignant diseases of the reticulohistiocytary system) or in high whole body hyperthermia, and particularly in the elderly.

Only in phases when the selective occlusion of the cancer tissue capillaries under hyperthermia is envisaged, as in the CMT concept 1977/82 [22, 23, 125], may it temporarily not be used, because oxygen counteracts endothelial swelling and thus also the irreversible vascular occlusion.

The time of recovery after infections with high fever is known usually to last several days. According to the measured values entered in Fig. 125, it can be reduced to just a few hours, when the increase in cardiac output and RMV which occurs in fever, is used for the O₂MT-mediated improvement of the blood microcirculation [234].

In high fever (40°C) pulse accelerations from, e.g. 70 to 100 per min occur, and the cardiac output (COP) increases from approximately 6 to 12 l/min. At a normal temperature (37°C) the same occurs in physical exertion with 75 watt. In this exertion, or at 40°C fever, an increase of roughly 7–27 l/min in the RMV is observed in untrained persons. Roughly the same increases in COP and RMV are the physiological prerequisites of the 15 min O₂MT quick procedure GK 2-I with physical exertion. The correspondence of these increases gave the author the idea of using the late phase of high fever for an O₂MT quick procedure GK 2-III with a roughly 25 min supply of 25 l/min pure oxygen (via a mask applicator with storage balloon). In order to improve O₂ utilization the combination preparation 'Oxygenabund', or its components, is given orally, as for all O₂MT variants, approximately 30 min before start of O₂ inhalation.

The summary of facts and measured results in the application of the O₂MT quick procedure with use of high fever can be found in Fig. 125.

Similar results were obtained for numerous other cases with high fever in various clinics acting under the author's advice.

This O₂MT quick procedure, which can hardly be surpassed in its simplicity, deserves great attention because of its multivalent effect:

1. Circulatory support of the patient with high fever (risk reduction);
2. Reduction of time of recovery;
3. Reduction of working hours lost (in the interest of the patient, the employer and the medical insurance);
4. Charging of the host's defense system.

2.1.4 No poisoning by O₂ in O₂MT when the O₂ flow and the procedure duration are correct

Although oxygen is a blessing in intensive care units, in modern anesthesia, in emergencies and in O₂MT, it must always be remembered that O₂ poisoning can occur with a too high concentration of oxygen, or with respiratory gas mixtures with more than approximately 65 vol% O₂. The safety from O₂ poisoning is a question of the dosage as regards concentration and time.

It is stated in [32] that "in order to exclude the possibility of O₂ poisoning, respiratory mixtures with an O₂ concentration < 60 vol% and an O₂ partial pressure < 450 mmHg (60 kPa) are applied in longer lasting isobaric O₂ therapy in adults. In the treatment of newborn babies and infants, respiratory gases are used, the O₂ content of which must not be greater than 40 vol%, and the O₂ partial pressure not greater than 300 mmHg (40 kPa). Treatment with pure oxygen must be limited to approximately 4 h under normal pressure conditions."

In all procedural variants of the O₂MT the prescribed dosage of oxygen lies far below the toxic limit. The longest uninterrupted O₂ application is 7 h for the "5-night cure". O₂ is applied here during sleep via a soft mask applicator with storage balloon, with an O₂ flow rate adapted so that the O₂ concentration in the alveolar space of the lung is only approximately doubled. In the 2–4 h applications of O₂ during the individual sessions of the 36 h O₂MT procedure, the O₂ flow is always so adjusted that the O₂ concentration in the respiratory gas always remains below 60 vol%. Thus the regulation reported from [32] is observed with an additional safety factor in these procedural variants.

Pure oxygen or respiratory gas containing roughly 90 vol% O₂ is used in the 15 min O₂MT quick procedure. The 15 min application here remains very far below the aboved named 4-h limit, however, even with several repetitions of the treatment. In the O₂MT obstetrics procedure GK 2-IV, the dose of pure O₂ is limited to 120 min.

Dizziness and cramp are typical signs of O₂ poisoning. Changes in the alveolar membranes can be found in the lung, which can become a cause of diffusion disorders, increase in the proportion of shunt blood and accumulations of fluid in the alveoli (lung edema) [235]. In addition to this the COP is reduced as a result of increased vagotonia, and the circulation in the brain and kidneys is reduced. Numerous enzymes of the intracellular respiration are influenced. Thus, for example, the oxidation of glucose, fructose and pyruvate is inhibited in hyperoxia. The dangers of longer-lasting inhalation of pure O₂ in terms of progredient lung damage (total lung fibrosis as final stage) are shown in [236]. When a (toxic) dose of virtually pure oxygen is given for too long, the host's cellular defense is no longer stimulated, but reduced [237].

No detrimental effects have as yet been observed with very frequent 15 min O₂ applications, nor in the successful respective O₂MT variant over large periods of time (e.g. 10 years). Reference [238, 238a] should be mentioned in this context: it was found here in the framework of lifespan determinations using the Hayflick method, that the maximal cell division number was reduced to approximately 5% in cultures of human diploid cells (strain WI/38/ when the O₂ partial pressure in the cells was excessively raised from its normal level of around 15 mmHg (2 kPa) to 150 mmHg (20 kPa).

A positive consequence of the lasting improvement in the O₂ status for the non-specific cellular defense is the promotion of the formation of peroxides in phagocytosing cells (cf. Table 43). In other areas of the organism (e.g. the lens of the eye), the increased formation of toxic peroxides or oxygen radicals could in theory have negative consequences. Such a view has occasionally been asserted against the O₂MT, but it was overlooked that the body has developed an efficient antioxidative protective system for such areas. Enzymes such as superoxide dismutase, catalase, and also glutathione and ascorbic acid are involved there. Investiga-

tions into this question were carried out in our Institute together with the Institute of Pathological Biochemistry of the Medical Academy of Dresden, by Klemm and Schaper [239]. The result was that immediately after O₂MT treat-

ment (variant GK 4-I) an *increase of 50% in the antioxidative protective system superoxide dismutase (SOD) is measured in the red cells*, with only moderate decline in concentration in the course of 30–60 days.

2.2 Increase in the O₂ utilization capacity in the tissue by means of drugs (1st step)

2.2.1 Drugs and their dosage

The increase in the O₂ utilization capacity in the tissue can be defined as the improvement in the O₂ exploitation in the tissues and cells by means of the discussed capillary wall mechanism

and drugs. The effect of this improvement is a reduction in the venous oxygen partial pressure PO_{2-ven} , i.e. an increase in the arteriovenous saturation difference $\Delta SO_2 \triangleq \eta$, with unchanged

Table 12 Substances to increase O₂ utilization capacity in the tissues

No.	Substance	Area of influence in the organism	Biochemical place of influence	Dosage		References (Remarks)
				mg/kg	mg/70 kg	
1	Thiamine (Vitamin B ₁)	Whole body	Controlling of substrate flow into the Krebs cycle	0.43	30	2, 4, 242 (main drug)
2	Dipyridamol	Whole body	O ₂ and glucose permeation (brain); 5% increase of blood flow (myocar.)	0.7	50	2, 4, 243
3	Magnesium orotate	Whole body	"Nucleic acid precursor", electrolyte carrier, brain cell	1.4	100	2, 4, 244
4	Thiamine (B ₁) Dipyridamol Magnesium orotate	No.1 2 3 Whole body	Combination preparation especially developed for O ₂ MT	Tablet Ø = 11 mm, 3 mm thick	30 50 100 180	Drug combination "Oxygenabund" (A. Herbert KG, Wiesbaden-Bierstadt)
5	Orotic acid (Vitamin B ₁₃)	Whole body	as for 3	1.4	100	2, 4
6	Pangamic acid (Vitamin B ₁₅)	Whole body		0.43	30	2, 4
7						
8						
9	Vitamin C	Whole body	Improvement in host's defense capacity	14	1000	2, 4, 245 (Advisable supplement to combination preparation no. 4)
10	g-strophanthin (perlingual from a 6% solution in the oleophile phase)	10.1 myocardium 10.2 blood-brain-barrier (BBB) and brain	co-use of lactic acid as energy substrate	0.09 0.17	6 e.g. 12 (simultaneously!)	146, 171, 179, 180 (pH raising effect) 182, 186, 187, 192

physical exertion. A compilation of drugs to improve the O_2 utilization capacity in the tissue can be found in Table 12.

Vitamin B₁ (thiamine) is used in all variants of the O_2 MT as the *main drug to improve the O_2 utilization capacity*. As a component of the cocarboxylase, it promotes the oxidative decarboxylation of pyruvate, which stems from the Embden-Meyerhof pathway, to acetic acid. This is then subject to complete oxidation to carbon dioxide and water in the citric acid cycle [240]. Thus vitamin B₁ increases the oxygen requirement from the substrate side and thereby its utilization capacity [241]. Thiamine is a naturally occurring substance in plants, animals and humans. In the form of thiamine pyrophosphate (TPP) it plays an important role in the terminal oxidative pathway of carbohydrates, as the coenzyme codecarboxylase. It thereby gains great significance for the energy turnover not only of the structures of the nervous system, but also for the musculature, especially the myocardium. It has long been known that the vitamin B₁ requirements are directly correlated with the intake of carbohydrates in food, and that not only a deficient supply of the vitamin in food, but most of all, chronic alcoholism, diabetes mellitus and gastric subacidity, lead to a relative vitamin B₁ deficiency. It was found in animal experiments (rats) that the first sign of TPP deficiency is a drop in the codecarboxylase concentration in the brain, which finally leads to a drop in the energy turnover. Vitamin B₁ substitution therapy has therefore been practised for decades, and still has a firm place in clinics today; the ageing person deserves particular attention here, as he is predestined to latent vitamin B₁ deficiency because of a frequently one-sided carbohydrate diet and an almost always existent gastric subacidity.

The O_2 MT, which is originally intended for the elderly individual, therefore falls back on thiamine and proceeds from the consideration of abolishing the limiting influence of TPP in the energetic metabolism in the brain and myocardium, by means of mild surplus medication (single dose 30 mg). The direct proof, using animal experiments, of the correctness of this assumption came from our group (cf. Fig. 133): combined with an increased O_2 offer, thiamine (hydrochloride) in the given dosage range is able significantly to raise the steady state concentration of the energy-rich phosphates ATP and CP in the rat brain. Thiamine thus evidently leads to an improvement in the O_2 and glucose utilization in the tissue.

A further substance used is *dipyridamol* (INN), which works via two different mechanisms. It increases the uptake and utilization of O_2 and

glucose specifically in the brain [246]. Further

more, in an increased dosage (2.2 mg/kg) the drug causes a roughly 5 % increase in the circulation (in the myocardium) for the duration of approximately 90 min [243, 247]. Dipyridamol was included in the therapy regimen of the O_2 MT in order to use the described pharmacodynamic effects, namely in the brain and the myocardium, which lead to an improved circulation and an increased O_2 (and glucose) utilization. Like thiamine, dipyridamol's action could also be confirmed by animal experiments (cf. Fig. 133 and literature): In rats given 0.25 mg/kg (s.c.), an increase in the steady-state concentration of energy-rich phosphates in the brain tissue was achieved when the O_2 offer was simultaneously increased. Dipyridamol sometimes causes headache. This drug cannot be used in patients who react in this way (only 30 mg vitamin B₁ and 100 mg magnesium orotate should be administered, but not the combination preparation "Oxygenabund").

Another substance used is magnesium orotate, which is known due to its favorable effects on the cerebral functions, namely due to a certain prevention of age-conditioned cerebral changes ("nucleic acid precursor") [244, 248, 249]. The Mg^{2+} ion is essential for both the plant and animal organism. It plays a central role in the intermediary metabolism of carbohydrates and lipids, in the activation of numerous enzymes, also especially in synthesis and transfer of the energy-rich phosphates. Its interrelation with vitamin B₁ (TPP) is also interesting here. Mg^{2+} was accorded particular attention due to its inhibitory effect on vascular sclerosis in conjunction with a reduction of the serum lipid level (activation of lipases and cholinesterase), and also due to the observation that a Mg^{2+} deficiency evidently promotes the ageing of the organism.

The combining of Mg^{2+} with two orotic acid residues (uracil-4-carbonic acid) to form Mg orotate is founded on the known idea that a better intracellular exploitation (electrolyte carrier) of the magnesium could thereby be attained.

Magnesium orotate has therefore gained a firm position in the basic therapy for degenerative cardiac and vascular diseases, particularly vascular sclerosis, and is used increasingly in the elimination of latent Mg^{2+} deficiency in the elderly. For this reason it was included in the therapeutic program of O_2 MT, after experi-

ments with animals in our group showed an increase in the energy-rich phosphates, in particular in creatine phosphate in the rat brain, under O₂ inhalation and an s.c. dose of 1.56 mg/kg orotic acid.

Vitamin B₁, dipyridamol and magnesium orotate with their standard dosage for O₂MT are combined in the "Oxygenabund" (manufactured by A. Herbert, Wiesbaden-Bierstadt, FRG) in a *single, easy-to-swallow tablet* with a diameter of 11 mm and a thickness of 3 mm. It can be seen from Fig. 126 in accordance with [250], that this drug combination caused a *drop in the mean $P_{O_2\text{-ven}}$ of 4.4 ± 2.0 mmHg*, 30 min after administration. This corresponds to a 6% gain in the O₂ binding capacity of the blood. The level of this gain, illustrated by Fig. 127, was the reason to suggest in [252] the *preceding administration of such a combination preparation in order to increase the effect of exercise training of all kinds*.

The example in Fig. 128 shows that the measured P_{O_2} increase in the tissue due to the pharmacological steps is to be regarded as a considerable contribution, alongside the effect of O₂ supply.

One drug which is given or can be useful as an adjuvant medication, usually in a high dosage and in conjunction with vitamin C, in various O₂MT variants (e.g. KA 1), is nicotinic acid. In its flush phase it increases the $P_{O_2\text{-art}}$ (Fig. 126) for approximately 50 min, and can therefore be used in special cases to achieve a higher $P_{O_2\text{-art}}$ under O₂ application at the start of the treatment cycle. A cup of coffee has the same indication and, as Fig. 30 above shows, a similar effect (with greater variation).

As a substance to increase further the O₂ utilization capacity specifically in the myocardium and in the brain, g-strophanthin is used [150, 155], the extraordinary pharmacokinetics of which were discussed in 1.2.3. It was seen that

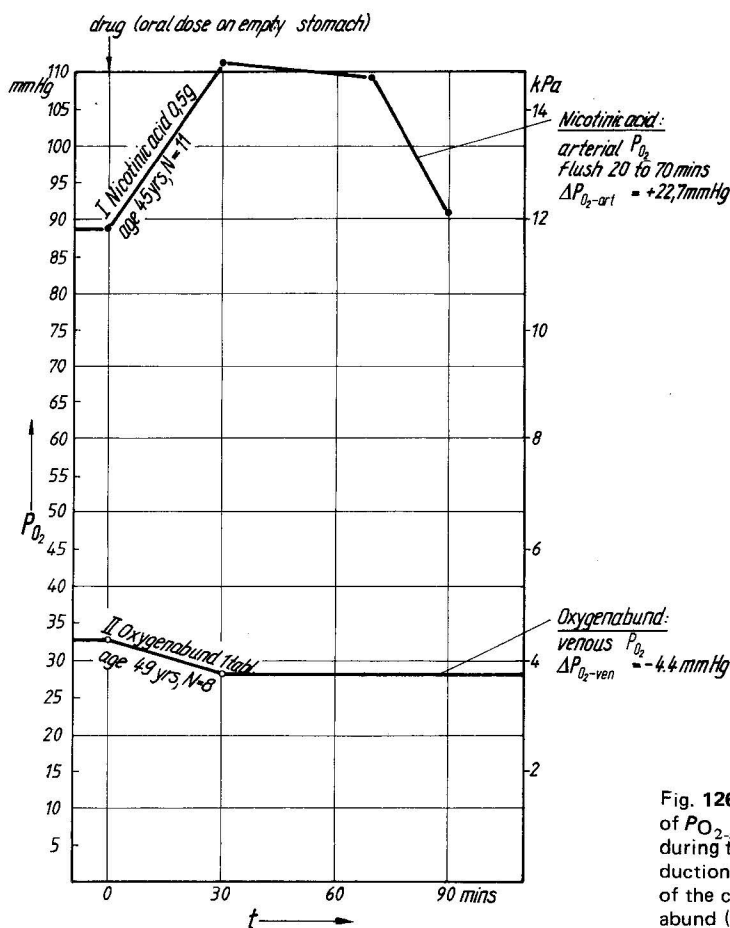


Fig. 126 Measurements showing the increase of $P_{O_2\text{-art}}$ by means of 0.5 g nicotinic acid during the flush phase (I) and a long-term reduction of the $P_{O_2\text{-ven}}$ by means of 1 tablet of the combination preparation Oxygenabund (II)

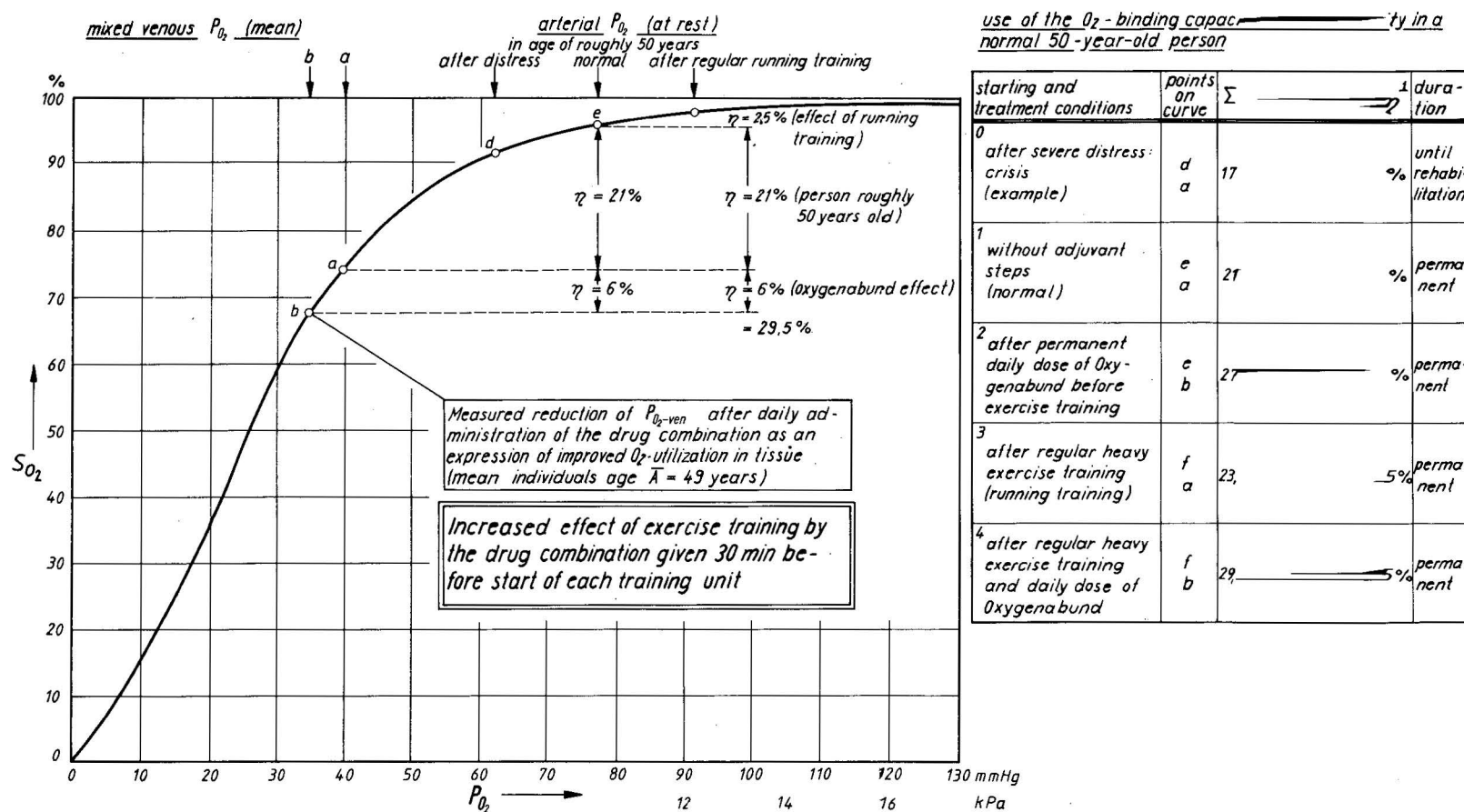


Fig. 127 The utilization coefficient η of the O_2 binding capacity of the blood in persons of roughly 50 years, without and with inclusion of the steps: Oxygenabund taken daily and regular heavy exercise training

¹ The η -increase by a factor ≈ 1.5 between condition 2 and condition 4 virtually corresponds to the increased O_2 transport to the body tissue, because the HMV between 1 and 4 only sinks a little

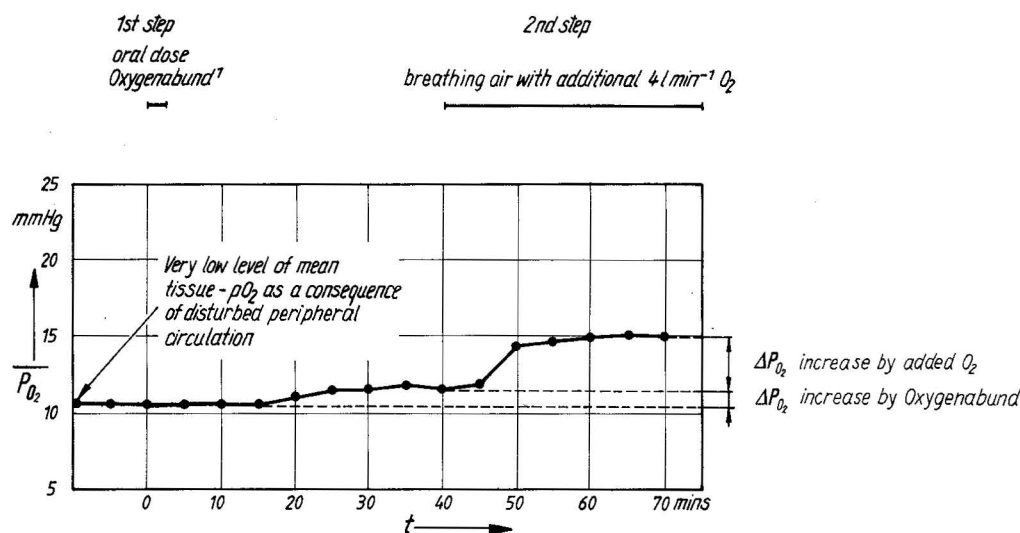


Fig. 128 Measurement, using a large-area P_{O_2} electrode, of the mean P_{O_2} level in the big toe of a 72-yr-old patient with circulatory disorders in the same leg, after oral dose (empty stomach, morning) of Oxygenabund (1st step) and after addition of 4 l·min⁻¹ O_2 to the breathing air (2nd step)

¹ Composition: 30 mg vitamin B₁, 75 mg Dipyridamol, 100 mg magnesium orotate

perlingually administered g-strophanthin has a reliable and strong effect, if the glycoside in an amount of 6 (or 12) mg and in a high concentration ($c = 6\%$ in the oleophilic phase), is put on the dried tongue.

It can be gathered from our present ideas on the temporal concentration course of g-strophanthin in the blood circulation, summarized in Fig. 129, that:

1. Since, under the given concentration conditions, the time constants of the binding of g-strophanthin to the receptors in the tissue are, according to [252], only fractions of a second, the effective bloodflow time to the receptors determines the elimination of the drug from the blood circulation (blood circulation time $t_c \approx 1.5$ min). This explains the extraordinarily small time constant of the evasion of g-strophanthin from the circulation, $\tau_{evas} \approx 0.5$ min [148].

2. For the binding of g-strophanthin to the receptors of the myocardial cell membrane, the given dose proportion is decisive, according to [252] and contrary to earlier ideas [179]. This means the triggering of the metabolic switching effect of g-strophanthin, postulated in [179] and proven in [146] (longer lasting, pH-increasing effect), as soon as a certain number of glycoside molecules (dose proportion, integral

value) are brought to the receptors, and not as soon as a certain glycoside concentration in the blood is exceeded.

3. In perlingual administration, between roughly the 2nd and 18th minutes after administration, a small, but after 6–10 min still highly cardio-effective proportion (e.g. 0.19 mg, almost the same amount as in i.v. injection) of the administered dose (e.g. 6 mg) goes directly into the blood circulation. This process can be termed "primary invasion phase" (I in Fig. 129).

4. When given perlingually, by far the greatest proportion of the dose (70–85%) is at first bound rapidly in the tongue tissue and stored there [252]. After a timespan determined by the dissociation time constant ($\tau_{diss} \geq 120$ min) [25], the bound high dose proportion (e.g. 5 mg) goes slowly into the blood circulation. This leads to the remarkable reincrease of g-strophanthin concentration in the blood circulation, specific to perlingual administration, beginning 2 h after application [253, 254]. It was shown in [148] that the evasion time constant increases from 0.5 min during the primary invasion phase, to 4 min during the second invasion phase. It follows from this that, in the dissociation process, a change occurs in the binding structure of the g-strophanthin molecule, which can explain the observed fact that the

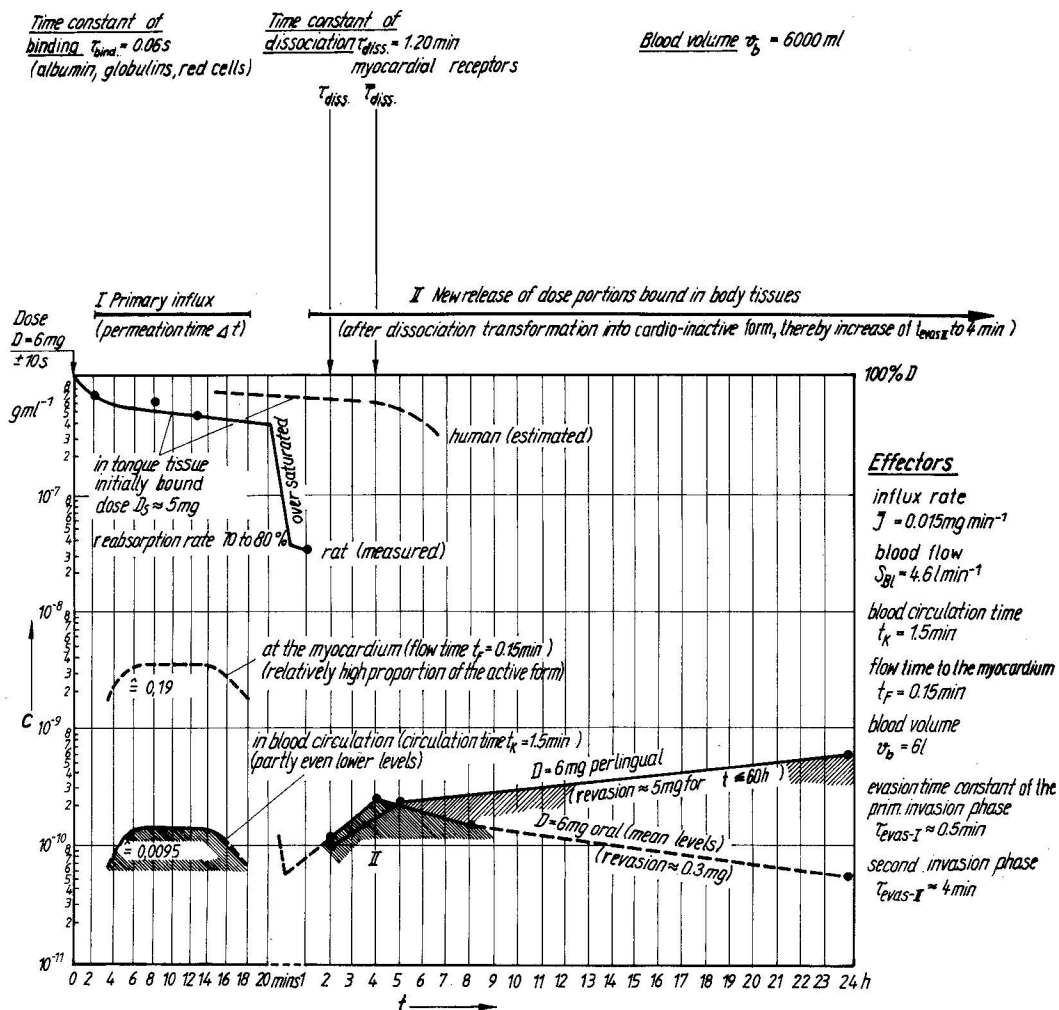


Fig. 129 Measurements and ideas derived from these [179, 180] of the time-dependent concentration profiles of g-strophanthin in the blood circulation after a perlingual 6 mg dose from a biteable capsule with a high strophanthin concentration [252] (Strodival special capsule). I. Primary influx phase (fast action with only slight variation of effect); II. Secondary influx phase (release, re-activation, inactivation) [148]

drug becomes cardioinactive and has low toxicity in the secondary invasion phase.

Perlingually administered g-strophanthin deserves great interest for O_2 deficiency in the myocardium because, when administered early enough by the patient himself, it can quickly ameliorate the dangerous reduction in the blood microcirculation or even eliminate it [122] due to its pH-increasing effect [148] in the deficiency area. The certain and rapid cardiac effect of g-strophanthin applied per-

lingually from a 6 mg – 6% preparation (Strodival special) has recently also been proven in a clinical study with large numbers of patients of an out-patient department (complete arrest of angina pectoris attacks within 5 to maximum 10 min after medication; failure rate only 15%) [147]. In special cases determined by the doctor (exercise ECG) the Strodival special preparation is also given 10 min before the start of the 15 min O_2 MT quick procedure, GK 2-I.

2.2.2 Experimental results of increase in the O_2 metabolism during treatment. Rise in concentration of energy-rich phosphates in the brain

The concentration of the energy-rich phosphates in the brain as an indicator of the increase in the O_2 metabolism in the tissue by means of steps of the O_2 MT. With Lohmann's

discovery of adenosine triphosphate (ATP) and the discovery of the creatine phosphate (CP), the basis was formed for the recognition of the comprehensive significance of the energy-rich

phosphates for the energy balance of the living cell. These phosphates play a decisive role in the anabolic and catabolic processes in the metabolism of carbohydrates, fat, proteins and nucleic acids, as well as in numerous energy-consuming cellular processes such as movement, transport of substrates, resorption and others. Thus every cellular activity is bound to a sufficient store of energy-rich phosphates, and correlates with an extraordinarily high turnover rate of these phosphates in the metabolic pathways involved.

When the individual cell performances are integrated to an organ system, e.g. the cardiovascular system, a considerable portion of energy needed by the nervous processes of checking and controlling is to be added to the cellular energy consumption. This proportion is recruited from the energy turnover of the nervous structures, particularly of the central nervous system. An increased content of energy-rich phosphates in the brain can therefore be seen as also representing a control reserve for the cardiovascular system. Since the provision of the energy-rich phosphates occurs mainly by the oxidative breakdown of glucose, the oxygen supply to the brain plays a predominant role, alongside the usually secured substrate offer. Because of these connections, determinations of energy-rich phosphates in the

brain should represent a sort of indicator of the potential increase in the O_2 metabolism in the tissue by means of the steps of the O_2 MT and, in particular, by means of the various drugs. Measurements of this type enable us to recognize useful drugs or drug combinations for the O_2 MT. They therefore belong to the arrangement and scientific foundations of the application program of this therapy.

The investigations [4, 242] were carried out on Wistar rats of 3 weeks and 6–9 months, with body masses of roughly 40 and 350 g.

The animals were put without further preparations in the equipment as in Fig. 130, which allowed the setting of various oxygen partial pressures in the inhalation air. Figure 131 shows a further view of the experimental set-up. By the use of O_2/N_2 mixtures, which continuously flowed through the box, sufficiently constant PO_2 levels could be set over a longer period of time, the level being constantly checked using a PO_2 electrode connected to a measurement amplifier. In this way it was possible to provide various proportions of oxygen in the inhalation air under atmospheric pressure. The temperature in all experiments was around 20–21°C, the relative humidity between 50 and 70%.

The investigation of a quantitative relation be-

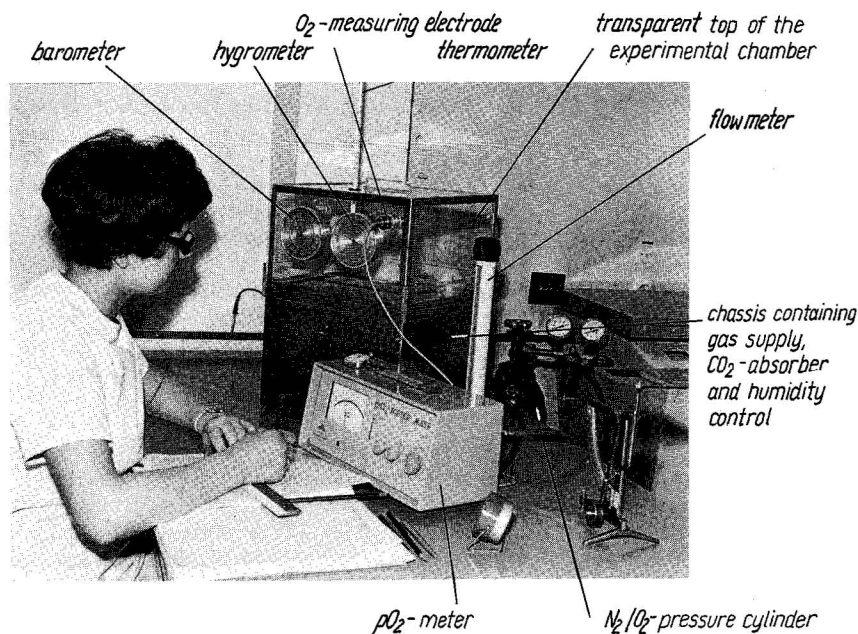


Fig. 130 Equipment for the adjustment of the PO_2 between 10 and 500 mmHg in the inspiration air for experiments with rats [4, 242]. 1 mmHg = $1.33 \cdot 10^2$ Pa

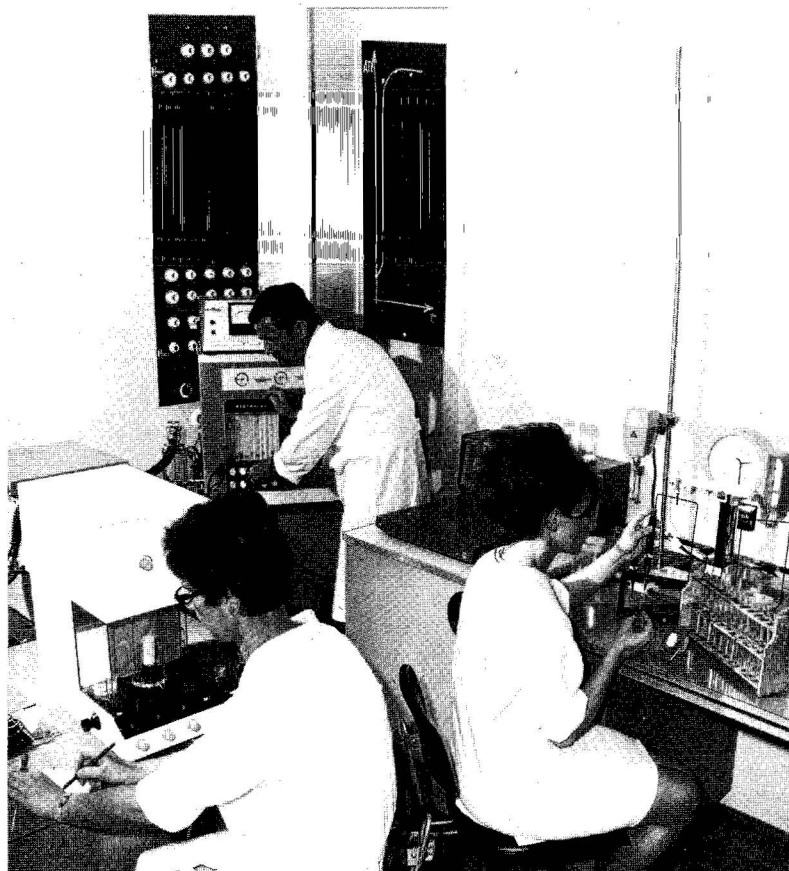


Fig. 131 Partial view of the physiological laboratory for research into the relationships between the P_{O_2} of the inspiration air as well as drugs increasing the O_2 utilization capacity, and the concentration of energy-rich phosphates in the brains of rats [4, 242]

tween the steady state concentration of ATP and CP in the brain tissue and the P_{O_2} of the inhalation air was based on the following experimental scheme.

From, in each case, three animals of the same sex, age and weight, one animal in each experiment remained at atmospheric P_{O_2} under otherwise constant conditions (control); the other two animals were placed in the incubator and were subjected for 120 min to a certain reduced or increased P_{O_2} . One of the two animals was taken after 120 min for the determination of ATP and CP (experimental animal 1); the other (experimental animal 2) was returned for periods of 10–60 min to the conditions of atmospheric or doubled P_{O_2} , and was further processed with the control animal. Thus three values could be obtained from one experiment: the $c_{ATP/CP}$ ratio of the control animal, which served as a reference value; the measurement value of experimental animal 1, which was related to the set P_{O_2} of the inhalation air in each case; and the measured value of experimental animal 2, which represented an index of the restitution rate of the stationary ATP or concentrations of the brain after the end of

the phase of relatively reduced oxygen partial pressure.

The animals were killed at the given times by quickly plunging their whole body into liquid nitrogen for a few seconds, then quickly removing the frozen heads, which were then again put immediately in liquid nitrogen. All further procedures were also performed in the cold. Adenosine 5-triphosphate (ATP), adenosine 5-diphosphate (ADP), creatine phosphate (CP), glucose (G), glucose 6-phosphate (G-6-P), lactate and pyruvate were determined in the extract of the brain samples. For a detailed presentation of all results see [242].

In the framework of the observations reported here we want to concentrate on the behavior of ATP and, to some extent, CP. The measurement of the ATP concentration in the tissue extract was carried out by means of an optical test (Warburg), using G-6-P dehydrogenase and hexokinase; CP was determined in the same test after addition of ATP and CP kinase. All tests were made in duplicate; the results were given as 10^{-6} mol/g wet weight. Over and above this the stationary ATP and CP concentrations were

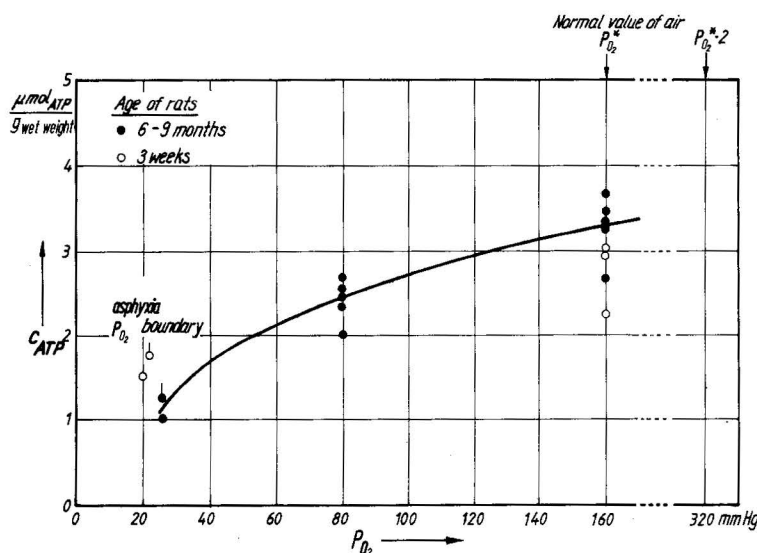


Fig. 132 Measurement of the stationary ATP concentration in the brains of rats as a function of the oxygen partial pressure P_{O_2} of the inspired air. (exposition time 60 min) [4].
1 mmHg = $1.33 \cdot 10^2$ Pa

calculated as a percentage of the standard concentrations of the control animal = 100 %.

Results on the dependence of the ATP content of the brain cells on the long-term P_{O_2} of the inhalation air. Measurements of the steady state ATP concentration in the brain as a function of the oxygen partial pressure are summarized for rats ($N = 17$) of the two age groups named, in Fig. 132. The influence of age could be seen particularly clearly in the case of the asphyctic P_{O_2} border. Here the 3-week-old rats had, with a lower P_{O_2} (20 or 22, as compared with 26 mmHg), an ATP concentration in the brain which was higher by a factor of about 1.5. This result confirms earlier findings, according to which older animals are more sensitive than younger ones to oxygen deficiency.

During the incubation period the animals remained under changed P_{O_2} long enough for it to be certain that steady state conditions had formed as regards the ATP concentration in the brain (120 min). The course of the curve obtained under these conditions shows a considerable increase in the ATP concentration in the brain when the P_{O_2} level rose from 30 up to 320 mmHg. The doubling of the P_{O_2} of the inhalation air from about 150 to 300 mmHg is a goal of the O_2 MT. In order to simulate with laboratory animals the older human organism with its cardiopulmonary performance reduced to 50% for example, rats aged 6–9 months were used and kept over a longer period of time at a P_{O_2} level that was roughly half that of normal air (80 mmHg). Under these conditions, the $P_{O_{2-art}}$ of the animals was around 70 mmHg.

Measurement of the increase in concentration of the energy-rich phosphates in the brain after the P_{O_2} of the inhalation air has been doubled and after administration of various drugs to improve the O_2 utilization capacity. According to [4], stationary concentration relations are reached after 30 min when the P_{O_2} is raised from 80 to 160 mmHg, and after 90 min when it is raised from 160 to 320 mmHg. Table 13 shows the extent of the increase in the concentration of energy-rich phosphates in the brain (correlation with the increase in O_2 metabolism) after the P_{O_2} of the inhalation air has doubled, and after administration of various drugs or drug combinations. These measurements prove that the dose of drugs to improve the O_2 utilization capacity (1st step of the O_2 MT) brings about a significant additional increase in the concentration of energy-rich phosphates in the brain, e.g. ATP from 140 to 160% with the simple combination of vitamin B_1 plus dipyridamol. The results given in the table form the basis for the choice of the drug combination according to type and dosage (e.g. combination preparation Oxygenabund) in the 1st step of the O_2 MT.

The slow fading of the concentration of ATP and CP, over a period of 4 h, which can be seen from the measurements compiled in Fig. 133, is surprising. This is a further fundamental effect of the O_2 MT. This result led to the 90 min O_2 MT variant being carried out immediately before severe stress. In this way, for example, extraordinary circulatory stability was recorded during brain operations of several hours' duration.

Table 13 Gain factors of the energy-rich phosphates ATP and creatine phosphate (CP) in the brain of rats 30 min after increase of the P_{O_2} in the inhalation air from 80 to 160 mmHg combined with the application of various drugs to improve O_2 utilization capacity. The high gain attainable with the drug combination (4) underlines the importance of even the first step of the O_2 multistep therapy. A high gain can also be derived directly from the measure-

ments in Fig. 126 (reduction of the mean venous $P_{O_2} = -4.4$ mmHg by the drug combination Oxygenabund containing Mg orotate, thiamine and Dipyridamol)

Drug	number of animals	appli- cation	time	Dose D mg/kg	total gain ATP	factor CP	drug gain factor ¹ ATP	CP	References, remarks
1 30 min sleep with normal P_{O_2} in the inhalation air					1.12	1.29	—	—	[242] values for middle-aged animals
2 30 min doubling of P_{O_2} in the inhalation air	30				1.40	1.62	—	—	(no drugs)
3 like 2, but with drugs:									[4]
3.1 Thiamine (vitamin B ₁)	6	i.m.	20 min before doubling of P_{O_2}	0.34	1.50	1.73	1.10	1.11	(main drug)
3.2 Dipyridamol (Persantin®, Curantil®)	6	i.m.	as 3.1	0.5	1.52	1.80	1.12	1.18	
3.3 Orotic acid (vitamin B ₁₃)	6	i.m.	as 3.1	1.56	1.47	1.84	1.07	1.22	(usually given as magnesium orotate)
3.4 Pangamic acid (vitamin B ₁₅)	6	i.m.	as 3.1	0.446	1.48	1.74	1.08	1.12	
4 Thiamine + Dipyridamol	6	i.m.	as 3.1	0.17 + 0.25	1.60	1.82	1.20	1.20	[4]

¹ Gain factor of P_{O_2} doubling subtracted

2.3 Increase in the blood supply of tissue (3rd step)

2.3.1 Significance of the blood flow for the attainment of a lasting improvement of η by means of the O_2 MT

The oxygen multistep procedures can only be successfully performed when there is a good blood flow in the tissue (good circulatory condition) and, particularly, when the circulation is increased by means of physical exertion or in some other way. For this reason the 3rd step, discussed in this paragraph, is an obligatory component of the O_2 MT. As was already discussed in Paragraph 1.1.1, the desired high-charging of the microcirculation occurs when the P_{O_2} in the venous part of the capillary network is increased during O_2 application to approximately 50–60 mmHg (6.6–8 kPa) (cf.

Fig. 3), and when, simultaneously, the circulating volume $\dot{Q}$ is high (cf. Fig. 57). Because of the influence of endothelial cell swelling on the narrowest capillary cross-section and therefore also on the circulating volume, these two parameters are functionally bound to each other. Nevertheless, it can be stated that *the higher nutritive capillary perfusion in the organs important for the elementary vital functions (lung, respiratory musculature, heart) the less oxygen and procedure time are needed to achieve the aimed-for high-charging of the microcirculation.*

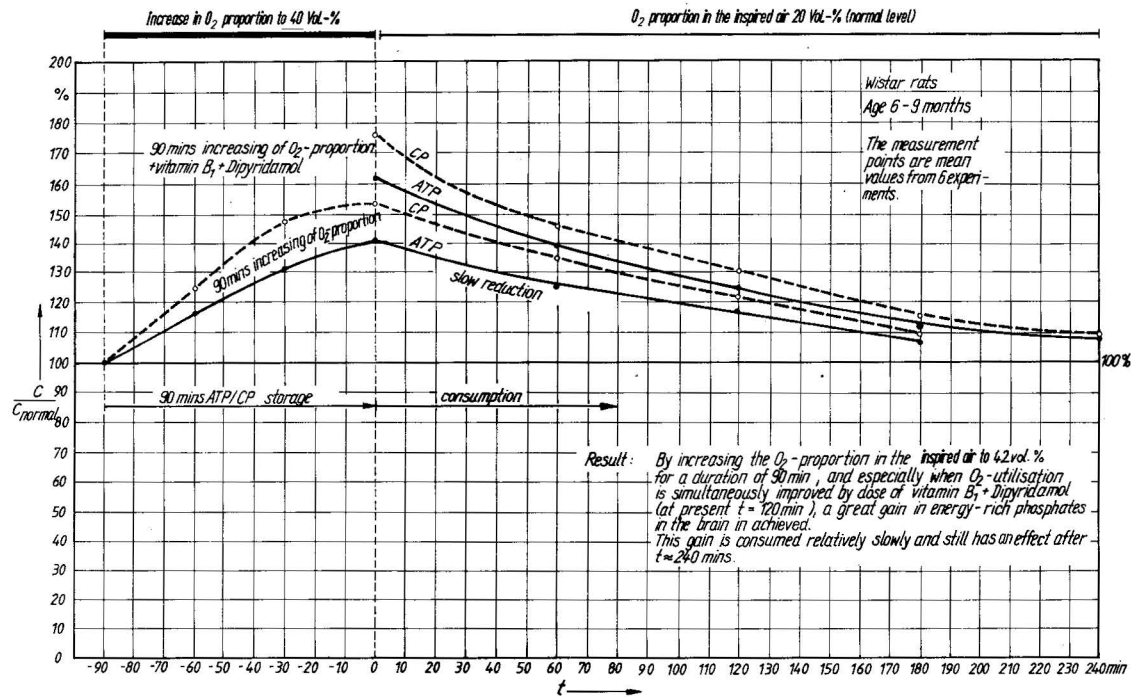


Fig. 133 The relative increase in concentration of energy-rich phosphates (ATP, CP) in the brains of rats during a 90 min O_2 M procedure (ATP-CP-storage), and measurement of the decrease in concentration after end of procedure [4]. Example of the "subsiding effect after treatment" (para. 5.1.3) in O_2 MT

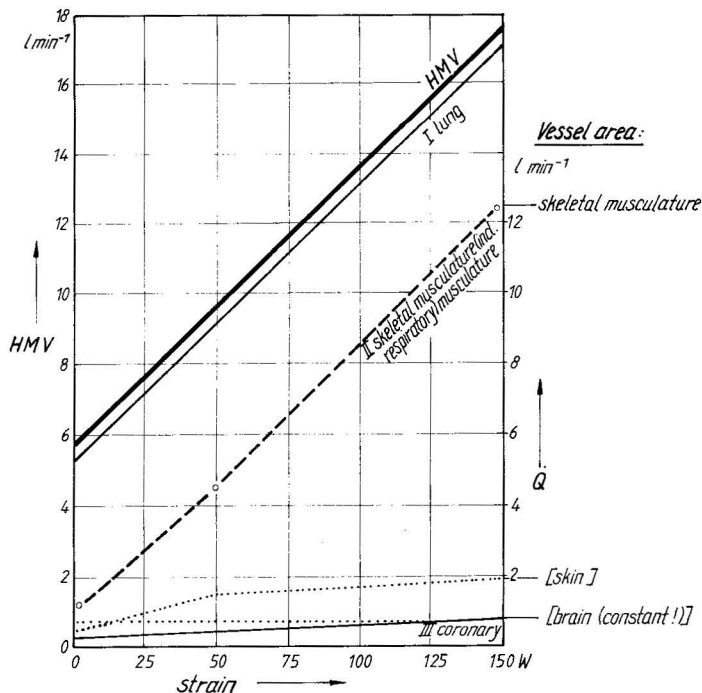
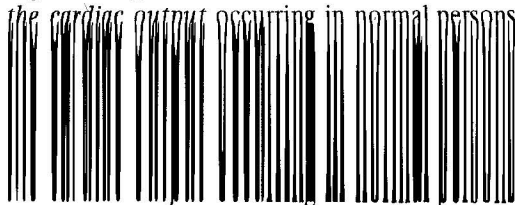


Fig. 134 Heart minute volume HMV and blood flow Q of the organs decisive for O_2 transport (to capillary endothelium), dependent on physical strain. Guidelines

2.3.2 Increase in the blood flow in lung and heart by means of physical exertion

Figure 134 gives information on the increase in



the cardiac output occurring in normal persons in increasing physical exertion (measured in watt). It can be seen from this presentation that the circulation in the two elements involved in the respiratory function (lung, respiratory musculature), and in the myocardium, increases by a factor of around 2 during physical exertion of 100 watts. As a rule, the $P_{O_2\text{-art}}$ then also increases with a typical course, as the example in Fig. 135 shows. An example of the approximate connection between cardiac output and pulse frequency f can be found in Fig. 136.

A very great increase in the RMV with exertion occurs simultaneously with the increase in cardiac output (see Fig. 137). At an exertion of 100 watts, for example, the RMV has risen by a factor of 4.7 compared with the level measured at rest. In order to ensure that the O_2 MT procedure employed has full effect, the flow of the respiratory gas mixture containing 40, 60 or 90 vol% O_2 is to be adapted to the RMV of the chosen physical exertion. When, at an exertion

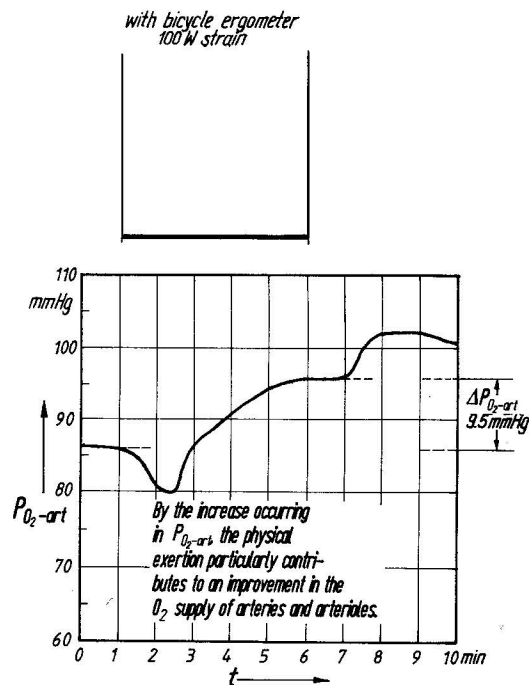


Fig. 135 Mean values of four transcutaneous registrations of the arterial P_{O_2} at a physical strains of 100 W in four healthy individuals. $1 \text{ mmHg} = 1.33 \cdot 10^2 \text{ Pa}$

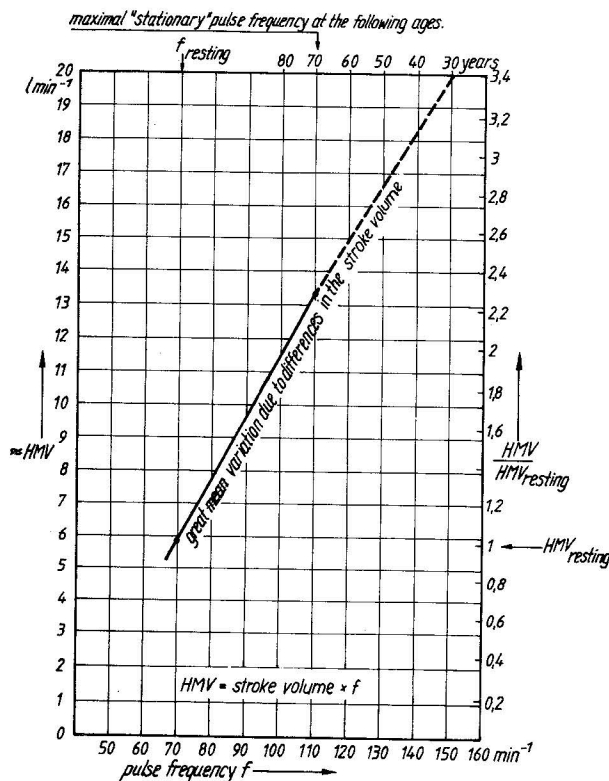


Fig. 136 Relationship between pulse frequency f and heart minute volume HMV. Approximate mean values at normal conditions according to [106]. The age-dependent decrease of the minute volume is reflected by the upper scale of the maximal "stationary" pulse frequency. In O_2 MT these values can be temporarily exceeded

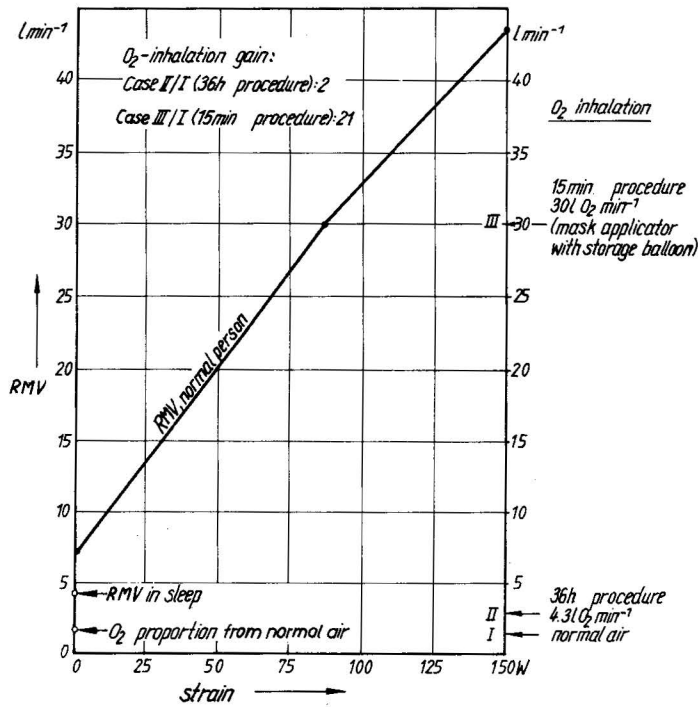


Fig. 137 Respiratory minute volume RMV of normal individuals dependent on physical strain; guidelines

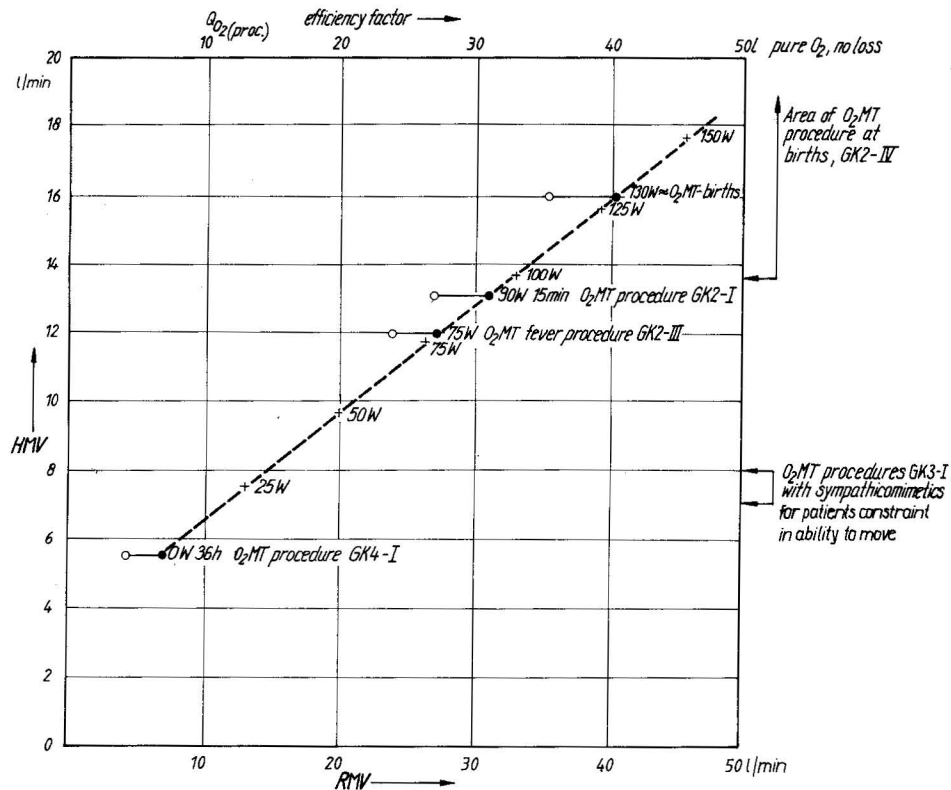


Fig. 138 Heart minute volume HMF, respiration minute volume RMV and O_2 flow rates needed for the different O_2 MT procedures ($Q_{O_2}(\text{proc.})$) in dependence on physical strain given in watts during various O_2 MT treatment variants

of 100 watts and application of pure oxygen (quick procedure), this adaption is established, the O₂ supply to the lungs, for example, is increased by the product $4.3 \cdot 4.7 = 20.2$ (1) com-

pared with normal conditions. In this example the amount of O₂, increased 20-fold, is to a large extent taken up by the lung. This explains why the named exertion can also take place in conditions of weakness.

The occurrence of an over-proportional increase in the RMV with increasing exertion (without application of O₂) is a sensitive sign for the reaching of the aerobic/anaerobic border of

exercise training. The relationship between cardiac output and RMV as a function of physical exertion and the pertinent O₂ flow rates of various procedural variants of the O₂MT is given in Fig. 138.

2.3.3 Increase in the circulating volume in lung and heart by means of drugs

In physically disabled or non-able-bodied patients, who are particularly in need of the O₂MT due to the long-term distress of "exercise deficiency", the increasing of the circulating volume $\dot{Q}$ by means of drugs presents itself as a solution. Substances which increase cardiac output (COP) for 2–6 h have been known for a long time, certain doping substances banned for competitive sportsmen, for example. Table 14 shows a compilation of the COP-increasing effect of various sympathicomimetics [256–259]. The increase in COP attained in this comfortable and well tolerated way does not reach the level attainable by physical exertion in fully able-bodied persons. It is sufficient, however, in

order to design O₂MT variants in which the number of sessions and the total time needed are greatly reduced compared with the parameters of the 36 h O₂MT procedure, variant GK 3-I (Fig. 138).

O₂MT procedures with increase in COP by means of drugs should always be carried out during the morning, as the long duration of the effect afterwards could otherwise cause sleeping problems. It should also be pointed out and noted that, due to the side-effects of these drugs (euphoria etc.) the patient's fitness to drive is reduced.

It is known that a stimulation of the sym-

Table 14 Different effects of various sympathicomimetics and psychostimulants

Parameters	Orziprenalin ¹ Alupent®	Amezinium Regulton®	Mesocarb Sydnocarb®	Amphetaminil AN1®, Aponeuron®	Dopamin analogues USA	
increase in cardiac, output	35 D ₁ = D ₂ = 20 mg	22 D = 30 mg	moderately increased	not influenced	~ 40	%
pulse rate	increased + 14 %	not influenced or reduced	hardly increased	hardly increased	increased	min ⁻¹
onset of effect	after 30 min (D ₁)	20	20	20		min
duration of effect	from 30 to 75 min (D ₁) (D ₂ necessary for a 2 h sitting)	300	300	420		min
drug type	β sympathico- mimetic	sympathico- mimetic	psycho- stimulant	psycho- stimulant	sympathico- mimetic	
effect	peripheral	peripheral	central	central	peripheral	
receptors	β	α and β ₁	CNS neurons	dopaminergic CNS neurons		
blood pressure systolic	increased	ampli- tude + 30%	increased	hardly increased	increased	
blood pressure diastolic	lowered	increased	not influenced	not influenced	lowered	
breathing	slightly increased	not influenced	centrally increased	centrally increased	slightly increased	

¹ Noticeable reduction of most side-effects when used in combination with the O₂ multistep procedure

pathicoadrenergic system with the aim of increasing the COP is accompanied by an increase in the O_2 consumption of the heart muscle. Functionally limited compensations in the framework of a chronically ischemic heart disease are therefore a contraindication, not only for the O_2MT variants with physical exertion, but also with drug stimulation of the COP. This also applies to arterial hypertonia (danger of provoking a hypertonic crisis), visual field contractions (glaucoma simplex), psychotic disturbances and prostate adenomatosis.

Sympathomimetics should only be prescribed to patients in the framework of O_2MT under observation of the relevant contraindications and instructions given in the respective pharmacopoeia, i.e. not in agitated psychoses, thyrotoxicosis, prostate adenoma, contracted visual field or in severe myocardial diseases such as cardiac insufficiency, severe angina pectoris etc., or in severe hypertonia. The interaction of beta blockers and the drugs mentioned must also be observed here.

In some patients with reduced functional cardiovascular reserves, the administration of such drugs will only be possible in the progression of an O_2MT treatment cycle or even not until a second O_2MT procedure, when a preced-

ing successful treatment has caused these reserves to have been built up again.

We selected orziprenalin (Alupent), examined in Fig. 139. The measurement of the increase in O_2 uptake after perlingual administration of one 20 mg Alupent tablet (D_1) shows that a sharp drop in the heart effect sets in 75 min after application. For this reason, in a session lasting 2 h, a further 20 mg tablet (D_2) is usually given at $t = 45$ min, to secure a sufficient Alupent effect until the end of the session. The interesting observation can be seen from Fig. 139 (curve I) that, as a result of the O_2 application, the otherwise occurring critical drop in QO_2 to below the expected level (curve II) does not occur. Thus the main side-effect of Alupent is eliminated. The organism's energy reserves are not critically drawn upon, because more chemical energy is formed in the first effective phase.

If the known relation between physical exertion and COP is used as a basis, the sympathomimetic of the stated type and dosage is then equivalent to an additional physical exertion for the heart of 30 watts as can be seen from Fig. 140.

Without the combination with steps 1 and 2 of the O_2MT , i.e. used alone, the sympathico-

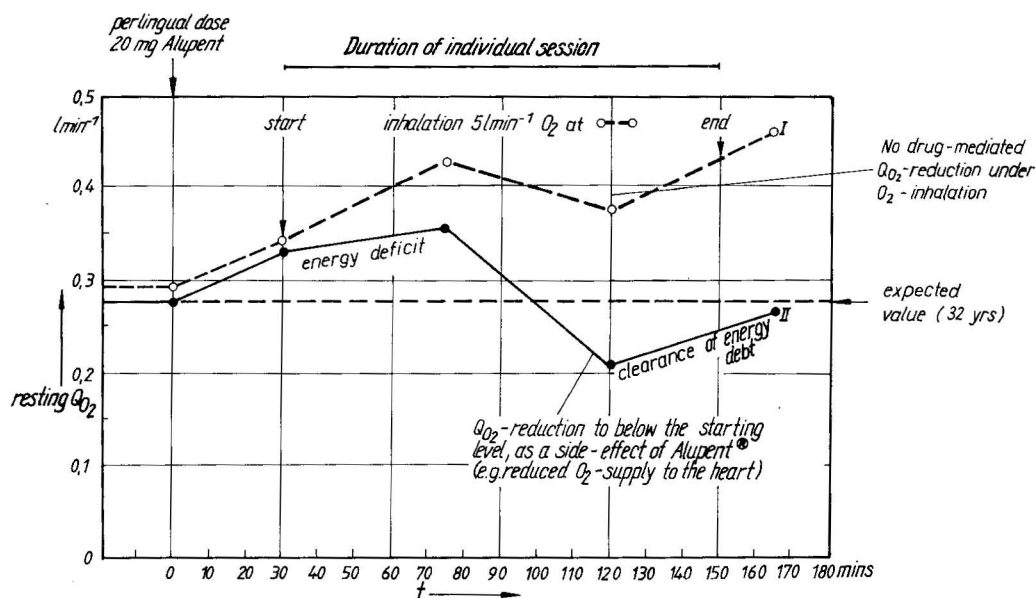


Fig. 139 Examples of the change in the O_2 uptake $QO_{2at rest}$ after a single perilingual dose of 20 mg Alupent with (I) and without (II) inhalation of $5 \text{ l min}^{-1} O_2$. In case I the O_2 inhalation was each time interrupted for 8 min for the determination of QO_2 . Result: the drop in QO_2 to below the starting level (normal level) between $t = 100$ and 120 min (main side-effect of Alupent) disappeared when additional O_2 was given according to the O_2MT program GK 4-II

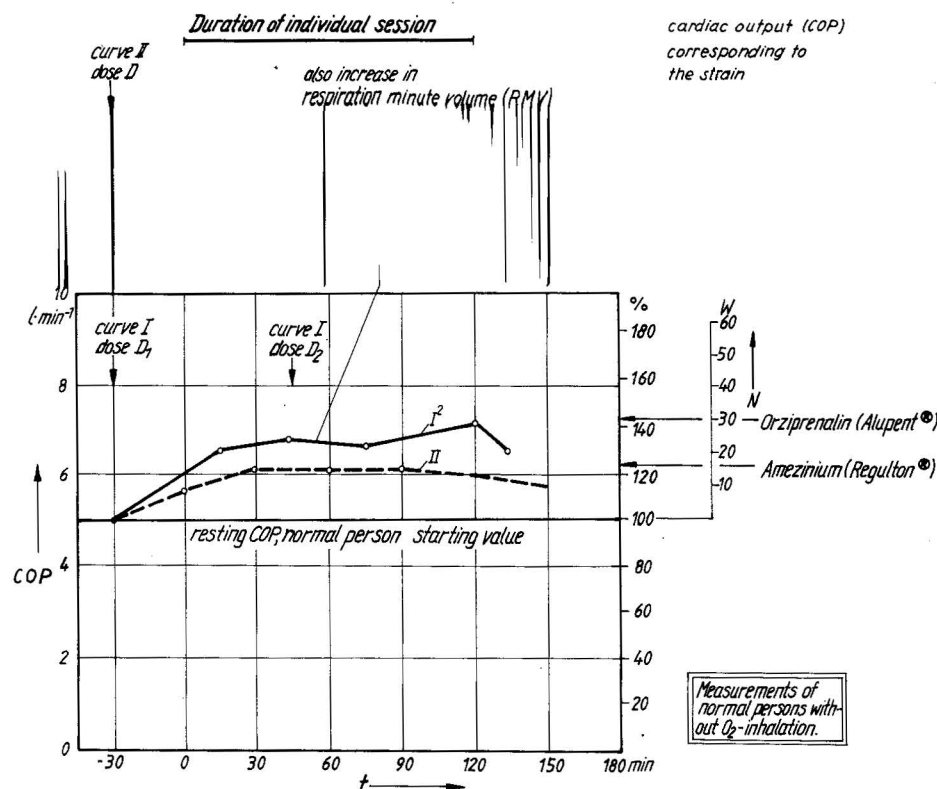


Fig. 140 Temporary increase in the cardiac output (COP) by means of sympathicomimetics, and their cardially effective portion expressed as a certain physical strain N . I = Orziprenalin (Alupent®), $D_1 = 20$ mg perlingual¹ at $t = -30$ min. $D_2 = 20$ mg at $t = 45$ min; II = Amezinium Metilsulfat (Regulton®) $D = 30$ mg oral

¹ Great weakening of most of the side-effects during the O_2 MT procedure

² This curve is even higher when $5 \text{ l min}^{-1} O_2$ is inhaled (except during determination of Q_{O_2})

mimetics generate an energetic debt in the human organism (feeling of weakness), which must be made up for after the action of the drug. Similar cardiac (side-)effects are known to occur in a series of cerebral stimulants, e.g. such as those of the amine group. A new era for the use of peripheral and central sympathicomimetics in combination with O_2 can be expected to emerge from this. Finally, it should be pointed out once more that the doping substance can be taken for the first time in this combination without negative effects. Inasmuch as doping substances mentioned here

leave a psychic dependence in the patient (problem of addiction), there is never any question of their use in the framework of the O_2 MT.

If this option exists, physical exertion is of course preferable as a natural method to increase COP. It is worthwhile in special cases to adapt to the physical potential by means of a suitable type of exertion (manual ergometer, e.g. from Ballert, Ennigerloh, FRG; special rowing devices etc.).

2.3.4 Normal and maximal blood flow of various organs

In efforts to increase the circulation in specific areas of the whole organism it is important to know to what extent the tissue blood flow in the individual organ can be increased by means of vasodilatory control. Figure 141 gives information on this. As is to be expected, the maximal increase in bloodflow occurs in vascular

areas in which the functional demands are subject to a particularly great change (skin, skeletal muscle, gastrointestinal tract, lungs, myocardium, liver, central nervous system). It is striking that the blood flow in the skin area can rise by a factor of up to 36. It is known that the size of this margin forms the basis of

the thermoregulation of the human organism by control of the heat convection. Figure 142 shows a more recent result on the increase in

brain circulation with increasing physical exertion, which was gained using the ^{133}Xe clearance method.

2.3.5 Increasing blood flow in specific areas of the whole organism

The temporary strengthening of the circulation during the 1st and 2nd steps of the O_2MT can lead to a strengthening of specific therapeutic effects for the other organs, too, and not just for the lungs and heart. We are thus confronted with the question of how, and to what extent, the circulation in specific areas of the whole organism can be increased. The answer to this question comes from the physiology of the regulation of the circulation. It is the task of

this circulation regulation to secure an adequate blood supply to the whole organism, both at rest and under changing conditions of strain. Most of the methods of artificially increasing tissue circulation on a temporary basis discussed later therefore amount to a general or partial increase in the strain on the organism.

For example, if the functional demands are increased in a particular area of the body, the

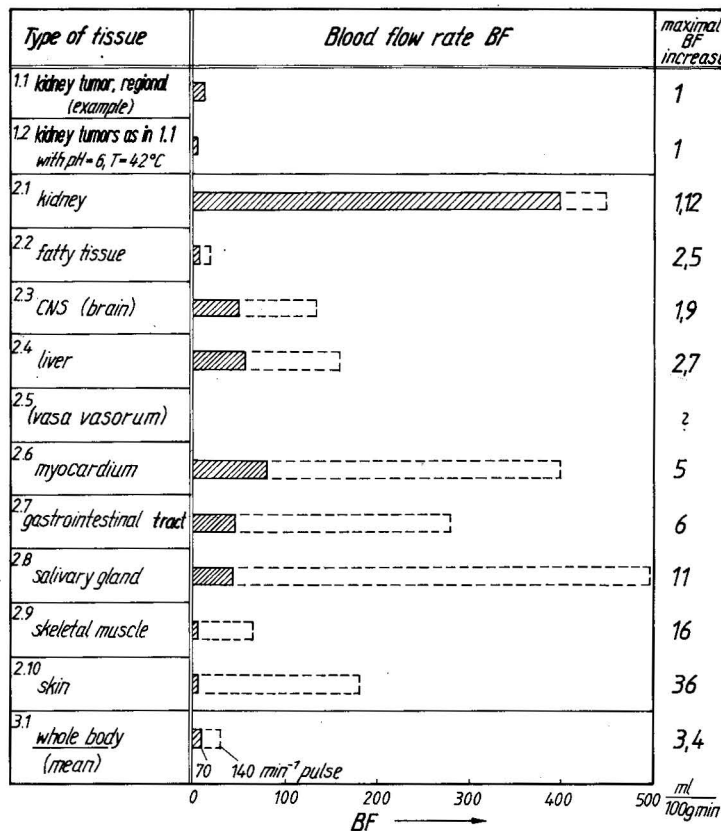


Fig. 141 Rate of blood flow in the circulation of the organs under resting conditions (hatched bars) and in maximal vasodilation (broken lines), for adults weighing 70 kg; modified according to [32]

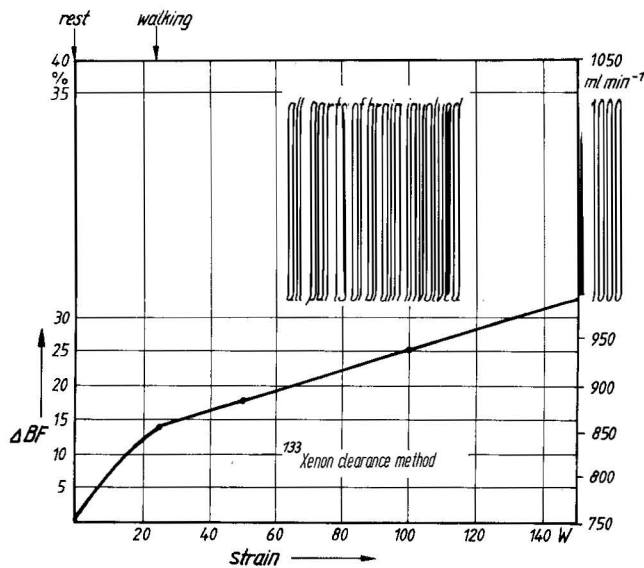


Fig. 142 Increase in brain circulation (blood flow BF) during physical strain according to W. Hollmann (personal communication of 3.8.1985)

organism adapts itself to the new situation mainly by an increased blood flow, that is, by an increase of the regional substrate supply. Because of the dependence of the flow resistance on the 4th power of the vessel radius (Hagen-Poiseuille's law), the regulation of the blood flow rate in the tissue by means of the related mediators occurs mainly by changes in the cross-sections of the vessels and, to a far lesser extent, by arterial pressure changes. The decisive vessel diameter is thereby mainly determined by the momentary state of contraction of the smooth vessel musculature in the

precapillary area (terminal arteriole segments, resistance vessels). This contractile state gives the vessel wall an active tension, the so-called vasotonia. An increase in the state of contraction causes a decrease in the vessel diameter (vasoconstriction) and vice versa, i.e. a decrease in the state of contraction causes an increase in the vessel diameter (vasodilation). By means of the control of the relative flow resistance in the so-called *precapillary sphincters*, the distribution of the cardiac output to the individual organ circulation, connected in parallel, and the strength of the blood flow within individual

Table 15 Blood flow in various organs and cardiac output at physical rest and during different physical strains. Adapted from [32] and Fig. 141

Vessel area	Blood flow (ml/min)				Remarks
	Rest	Light work (≈ 50 W)	Heavy work (≈ 150 W)	Maximal work	
Viscera	1400	1100	600	300	
Kidneys	1100	900	600	250	
Brain	750	880	1000	1400	855 at 25 W (walking)
Coronary	250	350	750	1100	therapy target
Arterial blood vessels (with vasa vasorum)	basic value	increased			therapy target
(Lung)	basic value	$\approx 1.4 \times$ basic value	$3 \times$ basic value	$4 \times$ basic value	therapy target
Skeletal muscle	1200	4500	12 500	22 000	(including lung musculature)
Skin	500	1500	1 900	600	
Other organs	600	400	400	100	
Cardiac output	5800	9500	17 500	25 000	ml/min
Arterial P_{O_2}	basic value	increased	strongly increased		

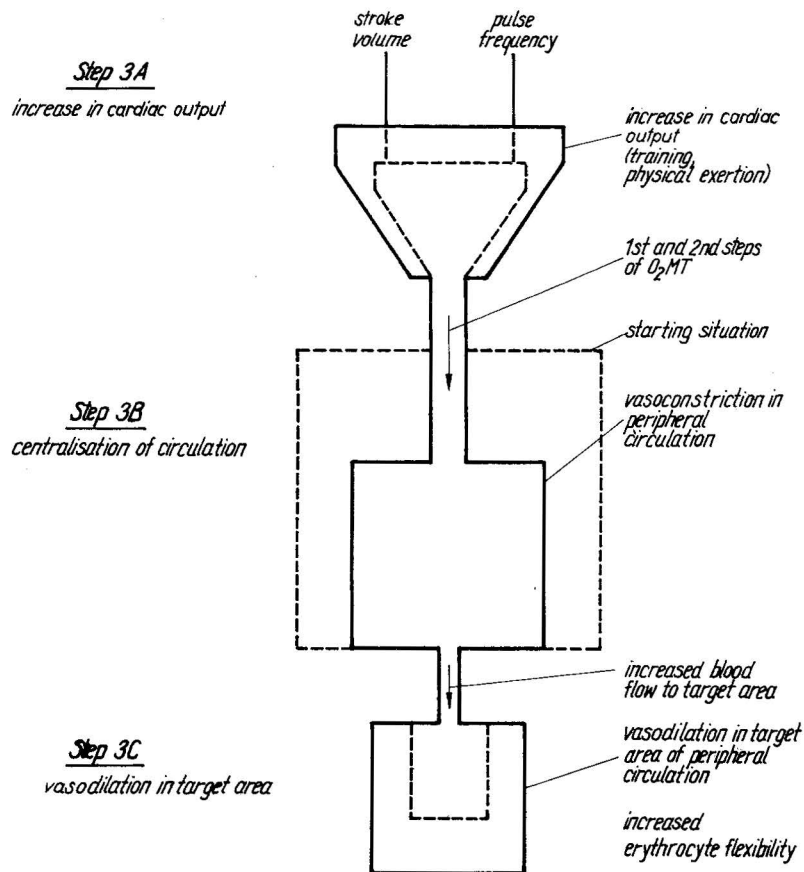


Fig. 143 Combination of measures to increase circulation in sections of the organism. Universal therapeutic principle to ameliorate local circulatory disorders

vessel areas are regulated. In most cases a change in cardiac output also occurs simultaneously with the processes, which direct the blood distribution; this change in COP balances the effects of changes in the whole circulatory resistance. Table 15 gives information about the *increase in circulation in the various organs as a function of physical exertion*.

An important area of application for the O₂MT is the *amelioration of local circulatory disorders* (local O₂ deficiency in the tissue). This special field of application stretches from the alleviation of *deficiency symptoms* after cerebral circulatory disorders (stenosis, thromboses, formation of emboli) by means of the fast application of suitable O₂MT variants, to the combat of chronic circulatory disorders in the brain and in the extremities. The therapeutic

principle of increasing the circulation in specific parts of the organism [260] shown in Fig. 143 should prove useful in the diminishing or even temporary elimination of an O₂ deficiency existing in limited areas of the organism. This principle, which is to be practised additionally in a further body section O₂MT variant (KA 2) after the O₂ status has generally been elevated by means of another appropriate O₂MT variant, amounts to a combination of an increase in COP (step 3A in accordance with the previous paragraph) with a redistribution of the blood flow in accordance with the therapeutic task in question. The redistribution of the blood flow is mainly achieved by means of appropriate influencing of the vasomotor activity in the *precapillary resistance vessels*, shown in Fig. 144. It has been recognized very recently that

Table 16 Information store for the method for removing quickly and temporarily local circulatory weakness by the combination of whole body vasoconstrictors (if necessary + physical exertion) with measures for the localized dilatation of precapillary resistance vessels in the affected body region. Increased effect by means of preceding O₂ multistep procedure (GK 4-I variant) with permanent raising of the η -value, and finally by means of the KA2 body sec-

tion variant of the O₂MT. Information store for the 3rd step of the KA2 variant

Measure for localized blood vessel dilatation in target area					Target body area of measure (remarks)
Type	Application	Special measure	Dose ¹	Duration of effect	
1 pharmaceutical	1.1 not localized, e.g. oral or i.v., but localized vessel dilatation in named body area	1.1.1 nicotinic acid (+ vit-amin C)	oral (sober) 0.5 g (0.5 g)	≈ 50 min (20 to 70 min after dose)	<i>head and throat</i> , little myocard, Table 32 (contraindications with hypertensive)
		1.1.2 pentaerythrityl tetranitrate (Pentalong®)	60 mg	60 min (20 to 80 min after dose)	myocard Table 32
		1.1.3 sympathicolitics e.g. yohimbine	14–70 mg		especially <i>kidneys and spleen</i> (aphrodisiac effect only at higher dosage)
		1.1.4 amyl nitrite or methyl-butyl nitrite	inhalation of the vapour	duration of artificial respiration	brain, myocard
		1.1.5 parasympathicomimetics			liver, joints
		1.1.6			
	1.2 localized by injection	1.2.1 procain injection	standard	≈ 20 min	joints
		1.2.2			
		1.2.3			
		1.2.4			
		1.2.5 arterial infusion of vasodilants		duration of infusion	
		1.2.6		duration of infusion	
	1.3 localized by application of skin irritants	1.3.1 cantharidin	standard	duration of application	also liver, gall bladder
		1.3.2 mustard oil	standard	duration of application	
		1.3.3			
	1.4 (increase of erythrocyte flexibility)	1.4.1 dose of drugs like O-(β -hydroxyethyl)-rutoside	5 mg 100 ml blood		decrease in reduction of flexibility in tissue with O ₂ deficiency with sunken pH (e.g. extremities)
		1.4.2 g-strophanthin (myocard)		duration of therapy	increase of sunken pH in the O ₂ deficient tissue
		1.4.3 hemodilution: slight reduction of hematocrit		≈ 1 day	whole body (in special cases, e.g. climbing highest mountains without O ₂)

Table 16 (Continuation)

Measure for localized blood vessel dilatation in target area					
Type	Application	Special measure	Dose ¹	Duration of effect	Target body area of measure (remarks)
2 physical	2.1 local hyper- thermia	2.1.1 water bath	$\approx 42^{\circ}\text{C}$	duration of hyperthermia	extremities
		2.1.2 hot cushion	severe reddening of the skin	duration of hyperthermia	organs and areas near to surface
		2.1.3 infra-red	severe reddening of the skin	duration of hyperthermia	organs and areas near to surface
		2.1.4 hot air breathing mask	$\approx 42^{\circ}\text{C}$ (humid air)	duration of hyperthermia	lung (Hirtz hot air-breathing mask with valve for O_2 addition)
	2.2 local high- frequency hyperthermia	2.2.1 microwave apparatus with wave-guide applicator ($\lambda_0 = 59\text{ cm}$)	$\approx 42^{\circ}\text{C}$	duration of hyperthermia	tissue near to surface (e.g. up to a depth of 3 cm)
		2.2.2 dekawave apparatus with eddy-current electrode ($\lambda_0 = 11\text{ m}$)	$\approx 42^{\circ}\text{C}$	duration of hyperthermia	tissue near to surface (e.g. up to a depth of 2 cm)
	2.3 local screen scanning HF hyperthermia: Selectotherm process	2.3.1 CMT-Selectotherm single-system installation	$\approx 42^{\circ}\text{C}$	duration of hyperthermia	tissue lying deeper beneath body surface
		2.3.2 CMT-Selectotherm	$\approx 42^{\circ}\text{C}$	duration of hyperthermia	tissues lying deeper beneath body surface
	2.4 local massage	2.4.1 manual massage		duration of massage	skeletal muscles
		2.4.2 vibration massage		duration of massage	skeletal muscles
		2.4.3 underwater ray massage		duration of massage	skeletal muscles
	2.5 local ultrasound fields	2.5.1 ultrasound (if necessary with focussing)	3 Wcm^{-2}	duration of sonication	bones, joints ($f = 900\text{ kHz}$, ΔT half-value depth = 2.2 mm in bone)
3 combina- tion of types 1 and 2	3.1	3.1.1 combination according to the case			combined with variants of the O_2 multistep therapy

For the treatment of peripheral circulatory disorders we cannot recommend strongly enough the combination of the O_2MT procedure (time: beginning of process) with the HOT* method mentioned in 1.1.10

¹ Given dosages refer to a body mass of 70 kg.

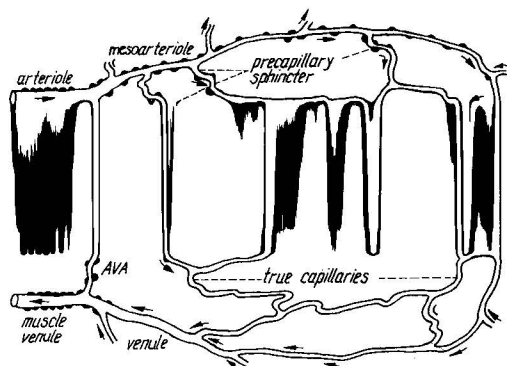


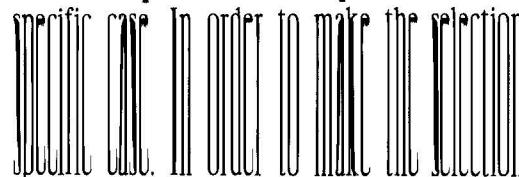
Fig. 144 Structure of the terminal network with its resistance vessels in the skeletal muscle [32]. The smooth vessel musculature which, as a contractile element, controls the vasomotor activity, is shown in black

prostaglandins exert a hormonal control also on the vascular system. These influencing measures are to be chosen so that, firstly, vasoconstriction occurs in many areas of the peripheral circulation, thus causing a kind of “centralization of the circulation” to occur (step 3B) and, secondly, so that vasodilation occurs in the area of the body with O_2 deficiency: target area (step 3C).

One way to achieve the redistribution is to inject i.m. a drug which reduces the cross-section of the resistance vessels in the whole organism (so-called vasoconstrictors, e.g. Pholedril, Effortil), and has a pressure-increasing effect for a limited time as it increases the peripheral resistance.

There are very varied ways to achieve vasodila-

tion in the O_2 -deficient area, which sometimes exist from the start, the type and combination of which depend on the therapeutic task in the



easier, Table 16 shows an “information store” with detailed commentary.

Dramatic improvements in the blood microcirculation in tissue with local circulatory weakness and thus also with reduced pH can be gained in conjunction with the O_2 MT by improving the rheological properties of the blood [262]. In particular, the HOT (UVR) treatment [262] and the administration of drugs such as pentoxifyllin (Trental) [263] and O -(β -hydroxyethyl)-rutoside (Venoruton) [114], which diminish the reduction in flexibility of the red cells in the O_2 deficient tissue, are to be named here. We must also name the method of temporary hemodilution [47] and methods which elevate a locally reduced pH (e.g. O_2 MT variants, g-strophanthin in the myocardium). In this the target of the drug and the site of action of the planned therapeutic measure must be carefully weighed, so that the strategic target is not missed due to overlapping and/or “stealing” effects.

Besides the pharmacological methods, the physical methods given in Table 16 below can often help in special cases to increase the circulation locally or regionally during the O_2 MT procedure (Paragraph 1.2.2). It is really true that all precapillary sphincters are dilated when a tissue temperature of $40-41^\circ C$ is reached.

2.3.6 Technical aids for the implementation of physical exertion

2.3.6.1 Technical aids for the determination of the physical fitness before and after O_2 MT

The great significance of exercise training to alleviate the critical reduction in cardiac output with advancing age has been pointed out in Paragraph 1.1.8.5. The determination of physical fitness can therefore be an important aid in the application of O_2 MT. Before we discuss this question we will say a few words about the immediate effect of physical exertion.

Paragraph 2.3.2 deals with the assessment of the increase in circulation in the target organs – lung and heart – in the individual patient case. The circulation of the whole organism follows from the relation of the cardiac output (COP) to body mass. The COP emerges from the product of pulse rate f and stroke volume. In the range $f = 70$ to approximately 140 per min, the stroke volume in normal individuals increases linearly in the ratio 1:1.3 [264]. The

connection between pulse and COP can therefore be given in a rough approximation. Figure 136 has already shown this connection. The pulse frequency which under conditions of rest usually lies at around 70 per min, can be greatly increased by physical exertion. The steepness of the increase in pulse rate with specific physical exertion is great in bad and only slight in good physical fitness. This relation is shown in Fig. 145 for males and females. Using the courses of the curves in Figs 136 and 145 it is possible to estimate approximate guiding values for the increase in the circulation of the whole body (and of the lung), or in COP by the increase in the specific physical exertion.

By contrast to the idealized presentation in Fig. 145, the pulse rate only increases linearly with the exertion at the beginning, and then approaches a maximal level (stationary pulse), the

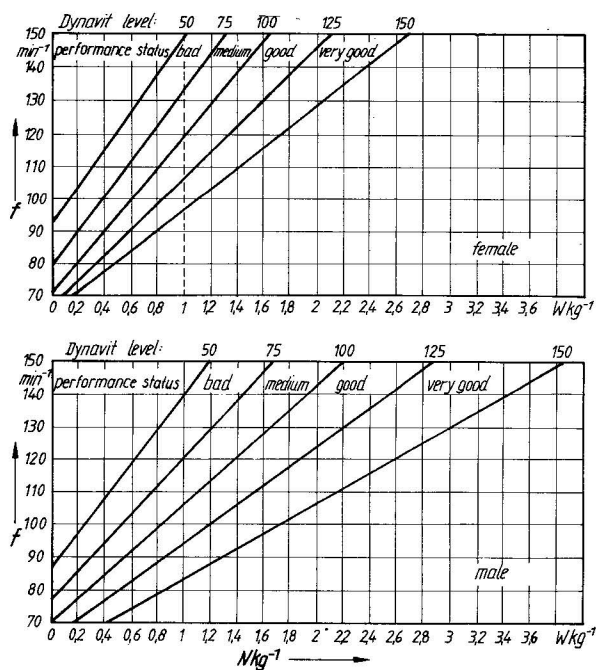


Fig. 145 Connection between specific exercise performance (watt per kg body mass) and the pulse frequency f at various performance levels of the human organism

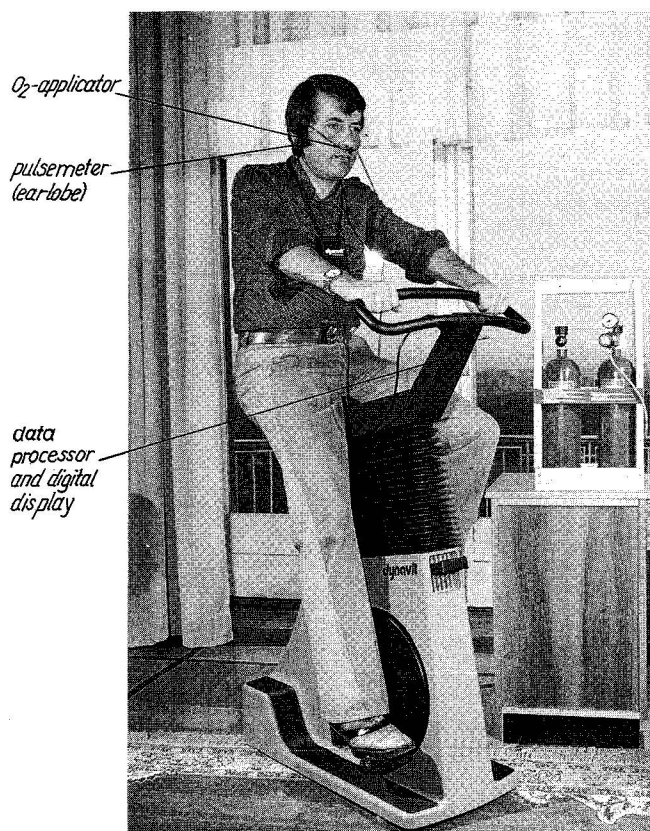


Fig. 146 Bicycle ergometer for defined strain and measuring of pulse frequency, performance status etc. during procedure of O_2 MT. (Keiper Training Systems, Rockenhausen/Pfalz, FRG)

absolute value of which depends on age, training condition and the PO_2 of the inhalation air. It is certainly not being too optimistic to

assume that in untrained persons at the age of

70 and under the conditions of O_2MT treatment (cf. Fig. 136), the pulse rate can be pushed by physical exertion (Fig. 145) up to 100 per min for a certain time. In this case the increase in COP, or in the circulation for the whole organism, compared with the levels existing at rest is approximately $BF/BF_{at\ rest} = 2.3$. A significant proportion of this increase serves to balance the increased O_2 consumption of the skeletal musculature caused by physical exertion (cf. Fig. 134).

The increasing of the blood flow in the tissues by means of physical exertion forms the obligatory 3rd step of nearly all variants of the O_2MT . The physiological aspects, which enable us to recognize the effects of PO_2 doubling of the inhalation air, and increase in tissue blood flow (effects which complement and support each other), have already been discussed in the previous paragraphs. Again, we envisage a longer phase with physical exertion in the *cardiopulmonal minimal training to increase COP*, in the program of the O_2MT . Finally, physical exertion has a decisive role to play in the fulfilment of the demand to lead on *energetic lifestyle* following O_2MT treatments.

An instrument for defined physical exertion with a fixed position, particularly suited for the O_2MT and the determination of physical fitness, is the Dynavit bicycle ergometer shown in

Fig. 146. By means of in-built electronics it facilitates the measurement of pulse under exertion and the determination of the performance

achieved in the training interval (e.g. 10 min)

and, using a microcomputer, it can codetermine a characteristic value for the current physical fitness (Dynavit value). In order to calculate this characteristic (Fig. 145), the personal data of the exercising person (age, weight, sex) are fed into the inbuilt computer by means of a keyboard; after 10 min of training the computer automatically shows the result from the performance achieved and the pulse frequency, in the form of a digital display. As can be seen from Fig. 147, in which the results of two typical experiments using this instrument have been entered, there was an improvement of the Dynavit value under (during) O_2MT . It is an interesting experience to observe during training how the stationary pulse rate drops (e.g. by 5–7%) as soon as the O_2 flow is switched on. According to this, the same defined exertion leads to a lower pulse rate, or higher exertion correlates with a constant stationary pulse frequency. The need for extra O_2 during exertion (especially in younger individuals) due to the high RMV is so great that the capacity of usual zeolite-operating oxygen producers is by no means sufficient, and so it is necessary to supply oxygen from pressure cylinders, for example.

A great increase in strain capacity under O_2 application is very striking and is seen in the effortless exceeding of the particular physical

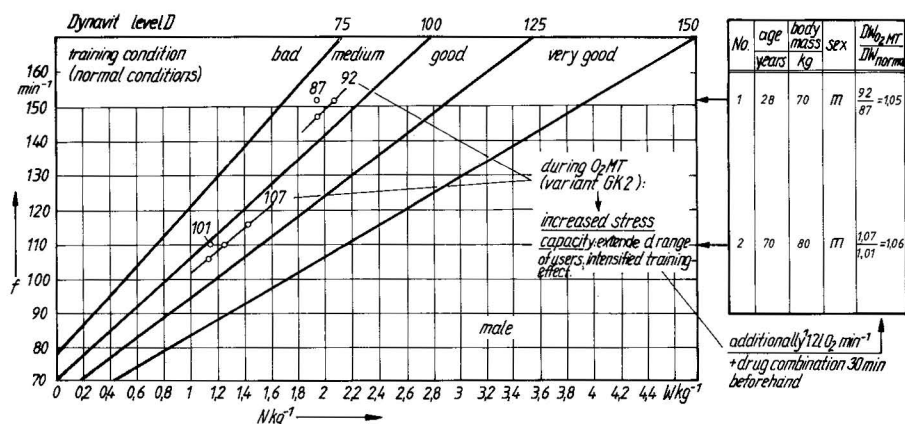


Fig. 147 Improvement of the specific exercise performance (watt per kg body mass) in dependence of pulse frequency f by means of simultaneous O_2MT in otherwise unaltered performance status condition. Typical examples. Dynavit level measured with Dynavit bicycle ergometer (Keiper Training Systems)

¹ Case of individual no. 1

performance capacity, which is otherwise limited by the individual age or possibly by any conditions of weakness. This means that patients (e.g. convalescents) who could normally not, or hardly, be expected to undergo exercise training, can be included in the circle of participants. This observation opens the way to a general shortening of convalescence, and also to the improvement of the state of health of chronically or acutely weakened patients, if the progressive exertion program is implemented under medical supervision.

The great increase in strain capacity or of the physical performance capacity under effective O_2 application with a flow of ≥ 30 l/min is of great significance in O_2 MT application of approximately 30–60 min duration during the process of birth [348], because the gain in strength helps the mother considerably, both in the phase before and during the expulsion of the child (shortening of the duration of birth etc.).

2.3.6.2 Technical aids for the stationary implementation of the physical exertion

The type of physical exertion depends in the individual case on the state of health of the patients and whether he has any physical disability and, if so, where this is localized in the body. The doctor must decide whether to use an O_2 MT variant with no or very slight physical exertion (e.g. the 36 h O_2 MT procedure GK 4-I) or the 15 min O_2 MT quick procedure GK 2-I with strong physical exertion; he must also decide what form the exertion is to take during the treatment.

The following alternatives can be chosen for the stationary implementation of the physical exertion:

- the bicycle ergometer (treadmill), with or without watt display,
- the step-climbing method (climbing test),
- the running belt method, with adjustable belt speed and inclination,

- manual (handle) ergometer,
- various hand instruments for selectable degree of exertion,
- rowing apparatus.

It is not always possible (or advisable) to preset a chosen exertion in terms of watts. It is often more reasonable to adapt the exertion to the resulting pulse rate. An electronic pulsemeter, such as the one in Fig. 148, makes such a procedure very convenient. With this the signal is gained from the earlobe using an earclip which contains the sensor, and the pulse rate is continually shown directly and in digital form. The least effort in order to achieve suitable physical exertion (e.g. used in one's own home) is needed when the O_2 flow prescribed for the procedure is first set with the aid of a flowmeter, and then the exertion is increased until



Fig. 148 Pulse meter/timer with digital display and earclip sensor (H. Kettler GmbH, D-4763 Ense-Parsit, FRG)

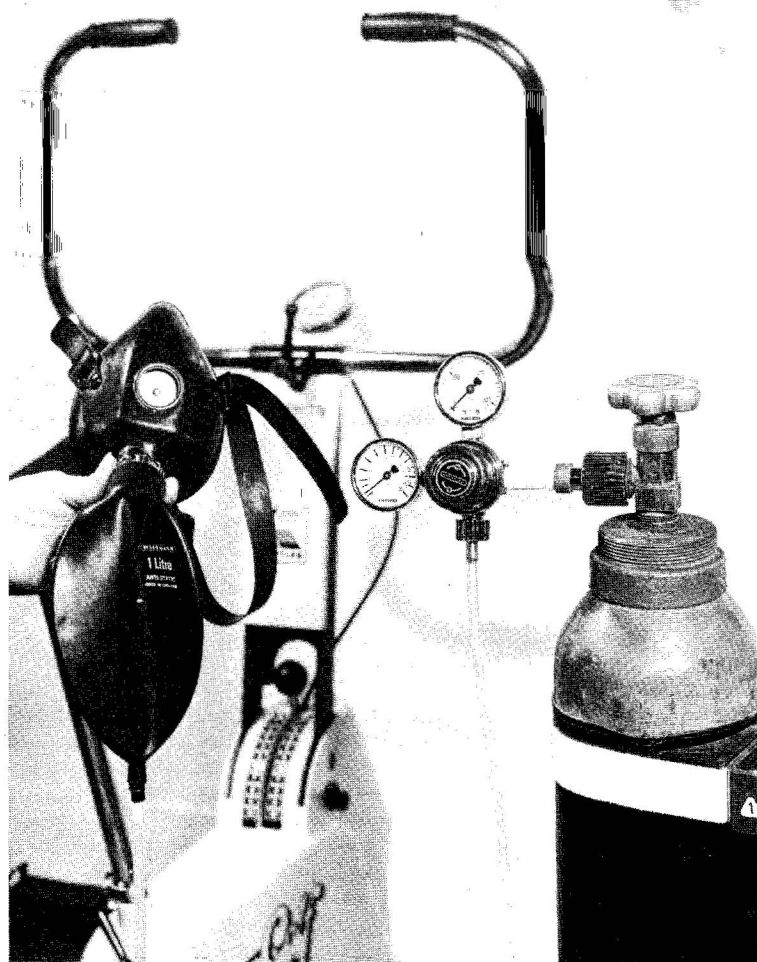


Fig. 149 Technical aids for the O₂MT quick procedure. Left, the low-loss O₂ mask applicator with 1 l storage balloon (type Weinmann); right, the 10 l pressure cylinder with reducing valve and special O₂ flow meter up to 30 l/min. In the background a home trainer with wattmeter (type: Golf, Kettler)

the storage balloon of the mask applicator is just emptied with every breath.

The form of physical exertion most frequently used in the 15 min O₂MT quick procedure is the use of a bicycle ergometer. The technical aids for this are shown in Fig. 149. Figure 150 gives a view of the scene during the implementation of the 15 min O₂MT quick procedure. In order to make the time pass more quickly for the patient, it is also possible to listen to music or verbal entertainment using a cassette player.

In the use of bicycle ergometers, WHO recommendations must be observed. The following are criteria for non-use and for particular caution:

Subjective criteria (general signs):

- increasing heart pains,
- feeling of dizziness or threatening faintness,
- numbness of the extremities or intermittent claudication,

- severe dyspnoea,
- muscular exhaustion.

Objective criteria:

1. *Clinical signs*

- severe cyanosis,
- cold, damp skin,
- cerebrovascular insufficiency.

2. *Hemodynamic signs*

- reaching of the age-matched pulse frequency limit according to Hollmann,
- the systolic blood pressure exceeds 230 mmHg,
- the diastolic blood pressure exceeds 140 mmHg,
- the RR amplitude is reduced by more than 20 mmHg,
- lacking rise in the systolic RR during more than two strain levels.

3. *ECG signs*

- paroxysmal arrhythmias (supraventricular or ventricular),

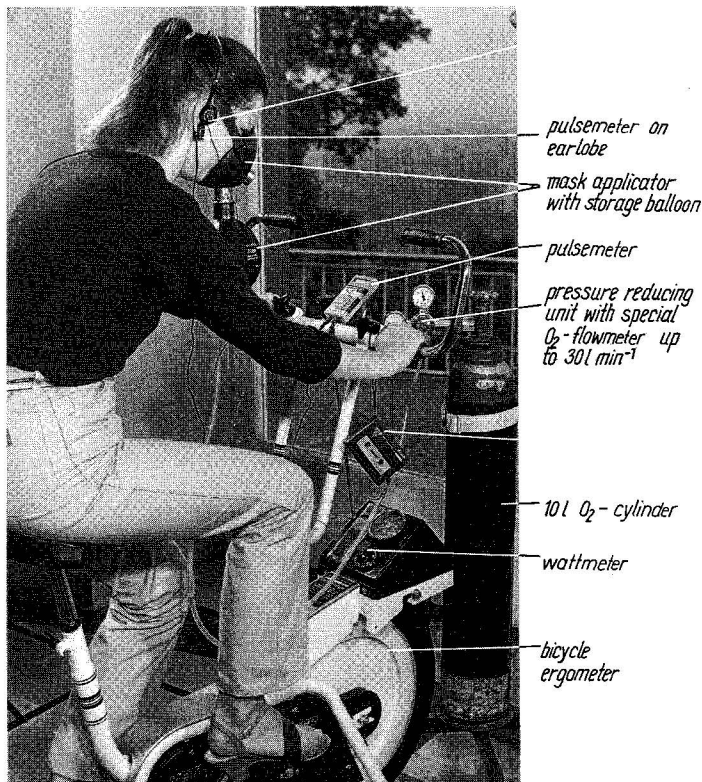


Fig. 150 Set-up for the 15 min O₂MT quick procedure for sufficiently mobile patients. Ergometer No. 7940 (H. Kettler GmbH, D-4763 Ense-Parsit, FRG), O₂ requirement = 450 l per process

- increase in the ventricular extrasystoles in the early phase of depolarization (more than 10 per min),
- atrioventricular or ventricular asystoles (except AV block, 1st degree),
- ST drop from the horizontal or descending type of more than 0.1 mV in the standard lead and 0.2 mV in the precordial lead compared with the ECG at rest.

4. *Combined signs*

- ST drop of more than 0.1 mV and unchanged systolic blood pressure with increasing exertion,
- rise in the diastolic blood pressure to over 130 mmHg with simultaneous reduction in the blood pressure amplitude.

Age-matched pulse rate limits according to Hollmann: $f = 220 - \text{age}$

Age groups	20–29	30–39	40–49	years
Pulse f	195	189	182	min ⁻¹
Age groups	50–59	60–69	70–79	years
Pulse f	170	162	145	min ⁻¹

No ergometric exertion in

- signs of decompensation,
- fixed hypertonia,
- severe angina pectoris syndrome,
- febrile infections,
- severe complaints or damage to the body's supporting apparatus.

For the implementation of the physical exertion by means of *stair climbing*, or the *step climbing method* [265, 268], there are no WHO recommendations. Figure 151 shows a simple aid for the stationary use of this method. The exertion is calculated according to the following relation:

$$N = h_{(m)} \cdot f_{(\text{min}^{-1})} \cdot BM_{(\text{kg})} \cdot 0.163 \text{ (watt)},$$

whereby h = height of step, f = number of steps climbed, and BM = body mass.

In some O₂MT centers (e.g. in the Klinik für Naturheilverfahren, Bad Füssing, FRG), there is also equipment for physical exertion by means of the running belt method and rowing.

Because of their chronic distress due to lack of exercise, the use of hand instruments during O₂MT is of particular significance for paraplegic

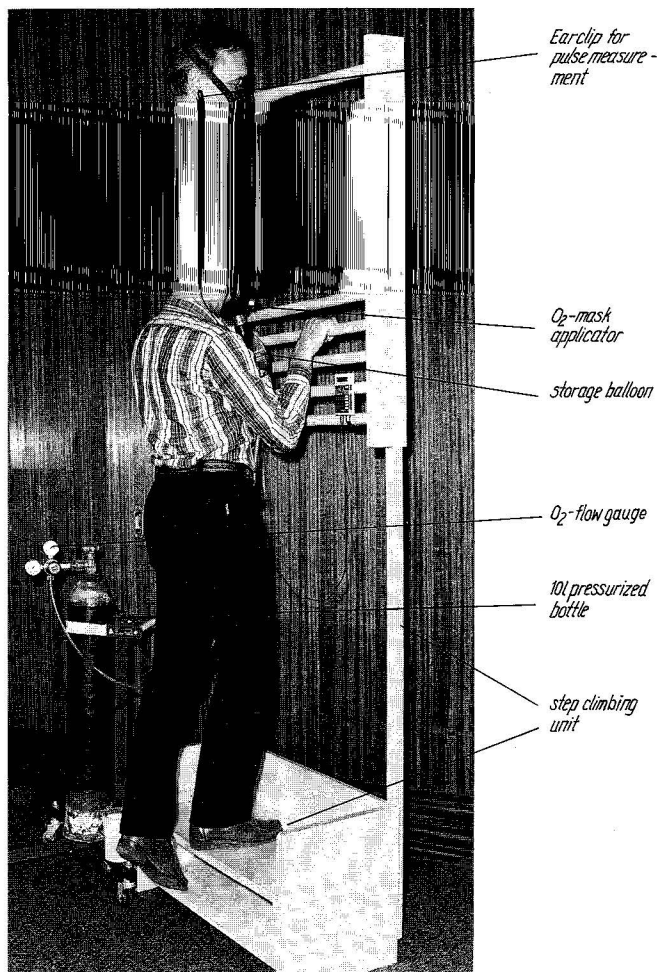


Fig. 151 Implementation of the 15 min O₂MT quick procedure with Kaltenbach's step-climbing unit. Adjustment of climbing frequency according to the prescribed training pulse frequency

and disabled patients. The simple manual ergometer with watt display, and hand instruments with selectable degree of exertion such as in Fig. 152 have been developed for this.

In connection with this attention should be drawn to a movable unit¹ for O₂MT, with which the physical exertion occurs with the aid of a swivelling ergometric part according to the crank ergometer principle (cf. Appendix).

2.3.6.3 Methods and aids for the implementation of physical exertion in exercise training and in transition to a more energetic lifestyle

It was shown in [37] that the deterioration of the O₂ status with advancing age can be traced back to the reduction in cardiac output. For this reason the combat of this reduction by means of exercise training is one of the most important measures for the maintenance of health in old age. The task consists of maximally increasing the cardiac output and afterwards keeping it high on a long term basis, but with the minimum amount of time and effort. In order to fulfil this demand, the O₂MT program plans *exercise training* on the one hand, and a transition to a *more energetic lifestyle* on the other.

The training must take place in both phases without application of O₂, as the desired training effect only occurs when the energy metab-

olism reaches the aerobic/anaerobic border (stimulus required for the sprouting of blood capillaries) [269, 270]. Because the training takes place without O₂ application it can be carried out either with stationary systems, or in a nonstationary way. For the same reason the training is not timebound to the interval of the main procedure of the O₂MT. Despite this, a *minimal training* [270] of 10 or 2 x 5 min without O₂ application was placed at the end of the

¹ Manufactured by Battert, Ennigerloh, FRG. The device consists of a 2 x 10 l pressure cylinder unit, O₂ flowmeter up to 40 l/min, electronic pulsemeter, exertion display etc. The crank ergometer is also suitable in most cases for disabled and paraplegic patients



Fig. 152 Technical aids for the implementation of short O₂MT variants for partially movement-disabled patients (e.g. bedridden). Use of the low-loss O₂ mask applicator with storage balloon and, in the foreground, a hand apparatus (impander) with adjustable strain. On the right a 10 l pressure cylinder with reducing valve and special O₂ flow gauge up to 30 l/min

Table 17 Several physical activities and their mechanical equivalents N on a bicycle ergometer (normal person, BW = 70 kg, height 1.80 m, male; approximate figures)

No.	Type of movement		N in watt
1	walking slowly	2 km/h	4
2	playing with children		15
3	walking	4 km/h	22
4	cycling without head wind	10 km/h	23
5	walking quickly	5 km/h	29
6	playing skittles (mean in time)		31
7	gymnastics		62
8	tennis (mean in time)		62
9	swimming (backstroke)	23 m/min	62
10	golf		64
11	dancing (foxtrot)		66
12	table tennis		70
13	pulse from 70 to 100/min (for < 80 years)		75
14	canoeing	126 m/min	93
15	pulse from 70 to 110/min (for < 70 years)		100
16	cross-country skiing	4 km/h	113
17	step climbing (height of steps 17 cm)	60 st/min	116
18	horse riding (gallop)		136
19	marathon running	9 km/h	142
20	swimming (breast stroke)	50 m/min	162

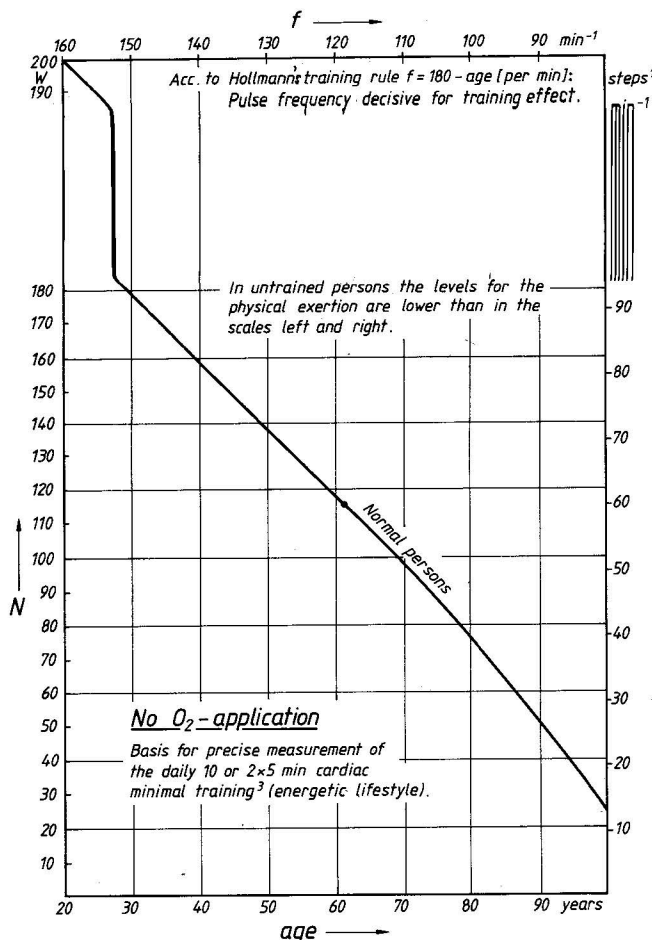


Fig. 153 The necessary physical exertion N or the pulse frequency f to be reached in order to attain the training effect². Right scale for exertion according to the step-climbing method

¹ Scale valid for 17 cm high steps. Normal person, body mass = 70 kg

² Reaching of the aerobic-anaerobic border

³ In the 15 min quick procedure a smaller exertion (60–100 W) can generally be applied

36 h O_2 MT procedure (variant GK 4-II), in order to use simultaneously the great amount of time necessary for this 36 h procedure, for the exercise training, too (increase in cardiac output) [37].

On average, normal persons reach the aerobic/anaerobic border (arterial lactate level 4 mmol/l) during physical exertion corresponding to the pulse rate according to Hollmann:

$$f = 180 \text{ minus age.}$$

The necessary degree of physical exertion, or the pulse rate that must be reached in order to attain the training effect, can be taken from Fig. 153. There exists great freedom in the selection of the method for the implementation of the exercise training. The stationary systems discussed in the previous paragraph, such as e.g. *bicycle ergometer, step-climbing equipment, running belts, manual ergometer, and rowing machines*, are the most suitable. In addition to this, if one is in very hilly areas, there is also the option of *walking along more or less steep paths, and other types of exercise*, as given in Table 17.

An indispensable aid, particular for non-stationary training, is an *electronic pulsemeter* with an accurate display and which does not hamper movement, such as the one in Fig. 148. The physical exertion is increased in the step climbing unit until the small electronic device, also photographed in Fig. 154, shows a pulse frequency in accordance with Hollmann's rule. If the patient is in possession of an electronic pulsemeter and lives in a multistorey block, then he can also using *normal stair-climbing* for his exercise training. After this commentary, further explanations on the use of the directly indicating pulsemeter in the use of other types of exercise are superfluous (cf. Table 17).

When any of the variants of the O_2 MT and the subsequent exercise training have successfully improved the value of η and the cardiac output, i.e. have significantly raised the energetic status of the organism, then the important thing is that *the person thus treated also makes use of the additionally gained energy and strength*. This means that the individual must change over to a more energetic lifestyle with types of

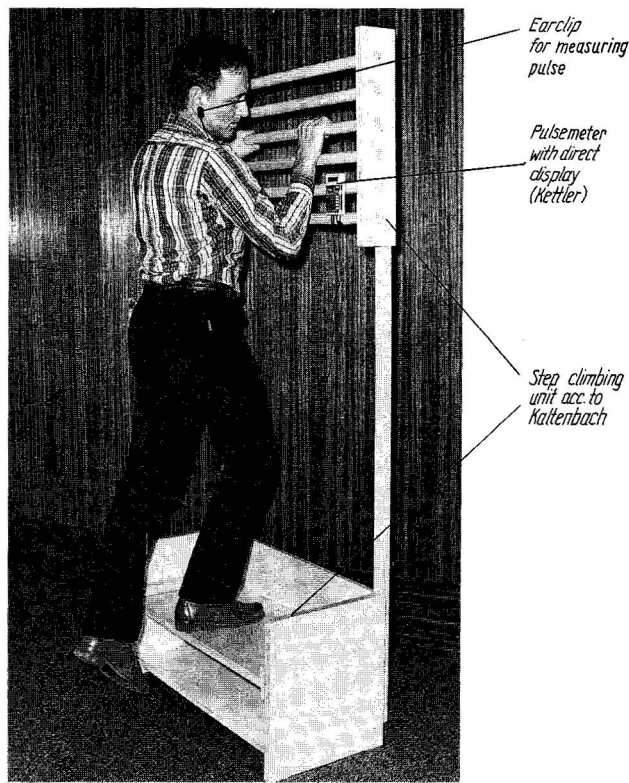


Fig. 154 Implementation of exercise training with pulse frequency adapted to age, using the step-climbing unit (without O_2 application: if possible 10–15 min daily). Climbing frequency selected so that the prescribed training pulse frequency is attained

exercise training adapted to his age [110]. If he fulfils this demand he can count on the measured improvement in his O_2 status remaining unchanged for months up to years. An energetic lifestyle, in the sense of our demand,

exists when *regular physical exertion of the level seen from Fig. 153 takes place for 10 min daily*, analogous to the exercise training and with any types of exercise that come into consideration.

2.3.7 Exercise training must be fun

It has long been our experience that people only do things voluntarily for a long time that are enjoyable. Independent of the aspects of O_2 MT already discussed, the following thoughts are therefore also of significance in the *individual designing of a permanently healthy and energetic lifestyle* under the conditions of our times. It was mentioned in the introduction to this book that lack of exercise is one of the greatest and still increasing dangers to human life in modern industrial states. The combat of this physical inactivity by means of suitable physical exertion, or the exercise training discussed, is therefore one of the medically most important demands of our days [266].

The American sports doctor and astronaut trainer Cooper even worked out a *score system*

for the amount and control of the daily training, for certain exercise programs (running, swimming, cycling, walking, running on the spot, handball) [9]. The *exercise counter* shown in Fig. 155 allows one to check, to a certain extent, whether enough “exercise units” [9] have been performed daily. This counter represents a meaningful variation of the well-known step counters. It gives relatively characteristic guiding values, if carried in a vertical position as near as possible to the middle of the body, e.g. on the belt or dress.

The drug combination for the raising of the O_2 utilization, Fig. 126, should always be taken before the daily exercise training in order to increase the effect [251].

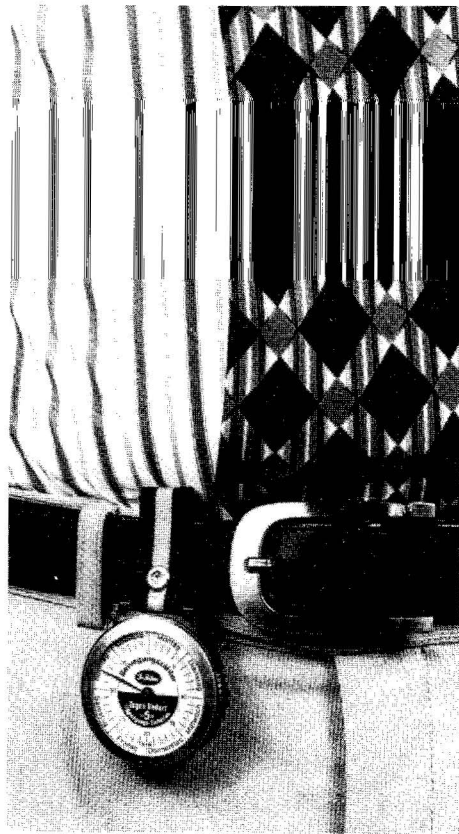


Fig. 155 Step counter for measuring physical performance in a time span of 1 week (according to Rihm, Weinheim/Bergstr., FRG)

In order to achieve a healthy lifestyle, especially also after the successful implementation of an O₂MT treatment, it is most important that the exercise training really is performed daily. Many variants of exercise training are boring and not very attractive. Even patients who are convinced of the necessity therefore neglect it again and again for a longer or shorter period of time, and this applies even more to patients who have not seen the sense of what they are required to do. We therefore make the demand here: *exercise training must be fun* [12].

What ways are there to design this general demand in such a way that the modern individual, with his chronic lack of time, enjoys fulfilling it regularly?

One form of arrangement of the exercise training should have in all variants the characteristic that *the time required is used multivalently*, e.g. either for the performance of useful satisfying activity or for fun, pleasure and enjoyment.

Examples of the first activity group are: strenuous garden work, e.g. mowing (scythe), digging etc., sawing and chopping wood, carrying heavy loads as help in the household, building etc. (do-it-yourself). Examples of the second activity group are: dancing and group sports where one's intellect is strongly included, e.g. tennis, football, hockey, and also sports which

lead the individual to experience the countryside, such as rambling in very hilly areas, long-distance running, skiing, cycling, swimming, rowing and horse-riding. Table 17 and Fig. 156 contain indications for the estimation of the *mean physical exertion in the various types of sport*.

As early as two decades ago, our friend Professor Th. Brugsch, the former head for many years of the 1st Medical Clinic of the Berlin Charité, dared in a lecture in Dresden to express the view, which only considered the well-being of men, that a young wife or girlfriend and "prolonged love" can also contribute significantly to the fulfilment of our demand. It is not difficult to guess a variant of this suggestion for women.

Mountain inhabitants are in the best position, as the regular overcoming of great differences in height, even carrying loads in the process, is part of their lifestyle.

The bicycle ergometer is one form of training in which the physical exertion can be administered in exact doses or kept constant, and thus the increase in pulse rate can be measured particularly easily. In order to make the rather boring use of this home trainer enjoyable, we recommend that the training be livened up by the simultaneous reception of radio and TV.

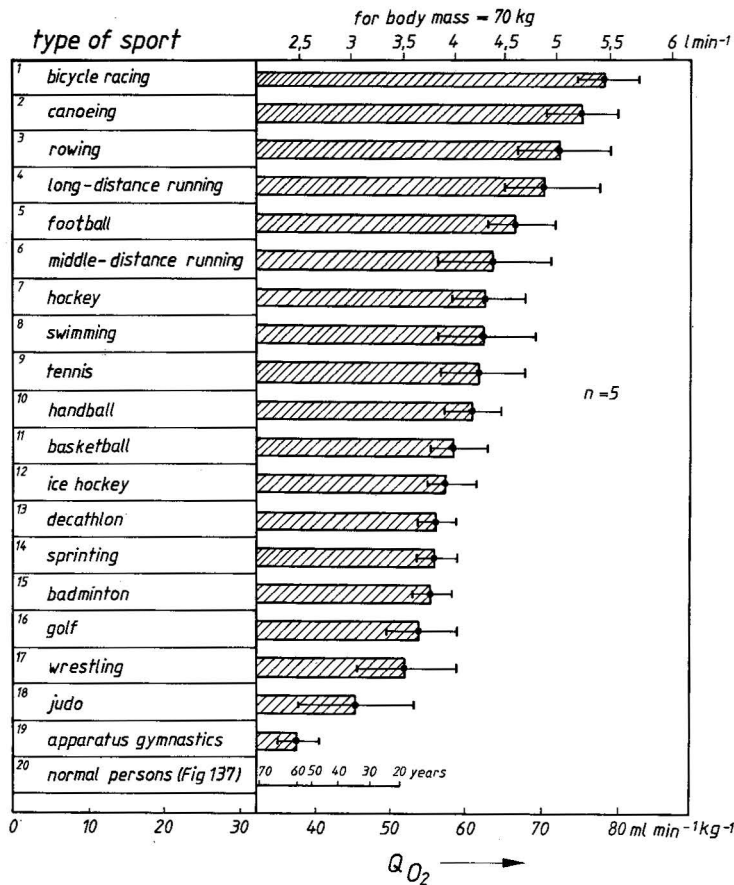


Fig. 156 Maximal O_2 uptake of top-class sportsmen of various disciplines according to Hollmann-Heck. The presentation gives an idea of the exertion of the organism in various types of sport and can help in the selection of a hobby sport suited to the individual case (age etc.)

It is to be expected that *preventive medicine* [271] will become a very significant area of the health service for the next few decades, in

which the simple question dealt with in this paragraph will no doubt play a great practical part.

2.4 Gain factors for the O_2 metabolism in tissues through the main steps of the O_2 MT and their combinations. Dynamics of the O_2 status

The improvement of the balance of oxygen in the tissue by means of the steps of the O_2 MT is also reflected in an increase in the mean PO_2 in the tissues [272]. Figure 157 shows measurements in the thigh of a rat with simulated older age, of the increase in the mean PO_2 in the body tissue with an increasing number of steps of the O_2 MT. These measurements were performed using microelectrodes, the technology of which will be discussed later. Figure 158 shows similarly programmed measurements performed with great care on a 32-year-old volunteer. Due to the age, which is still relatively low, the PO_2 gains in the skin tissue are not

quite so great as under the conditions in Fig. 157. These examples give quantitative indications of the improvement in the O_2 situation in the tissue during treatment by means of the 1st and 2nd steps of the O_2 MT. The greatest increases in PO_2 occur in the PO_2 diffusion system of the lungs and in the walls of the arterial vessels. The use of these facts for the combat of arteriosclerosis is discussed in Paragraphs 5.2 and 5.3.

For the special cases of the alveolar-capillary diffusion system of the lung, and of the walls of arteries and arterioles, it should be pointed out

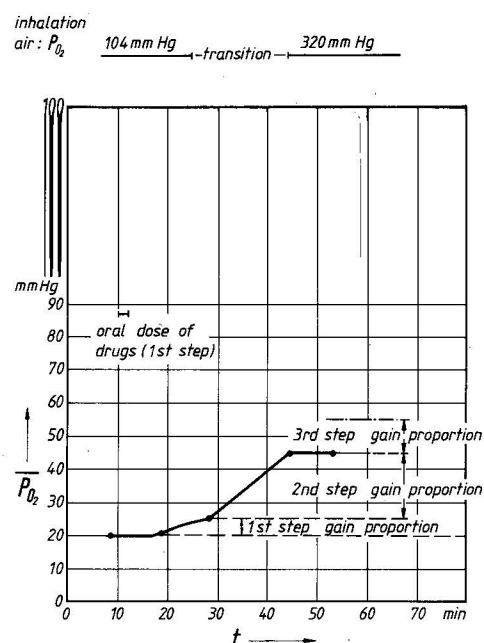


Fig. 157 Measurements, using PO_2 microelectrode, of the increase in the mean PO_2 level in the thigh of a rat, with increasing number of steps of the O_2MT [272]. Small area measurement. Simulation of higher age through reduction of PO_2 of the inhalation air to 104 mmHg at 30 °C room temperature

that, during the O_2MT treatments, the alveolar and arterial PO_2 , which is decisive for the oxygen diffusion from the alveolar space to the lung capillaries, or from the lumen to the vessel

walls, is increased to 160–500% of its normal level, depending on procedural variants (cf. e.g. Fig. 7, whereas physical exertion only brings about an increase of approximately 10%. In this special case the *gradient of O_2 diffusion during the O_2MT* therefore has a superiority of the factor 16–50. This is a factor which must be related to a strongly pronounced increase in the O_2 metabolism in the tissue layers named.

The measurement of the two resting PO_2 levels has been greatly neglected up to now because their great dynamics and reactivity, which are described in detail in this book, were not, or hardly, known, and because there were no simple, reasonably priced PO_2 meters. Added to this was the fact that, in the case of the PO_{2-ven} , at rest, it hardly seemed possible to gain this value on a routine basis and with sufficient accuracy (cf. Fig. 14). The situation has now fundamentally changed. The many meas-

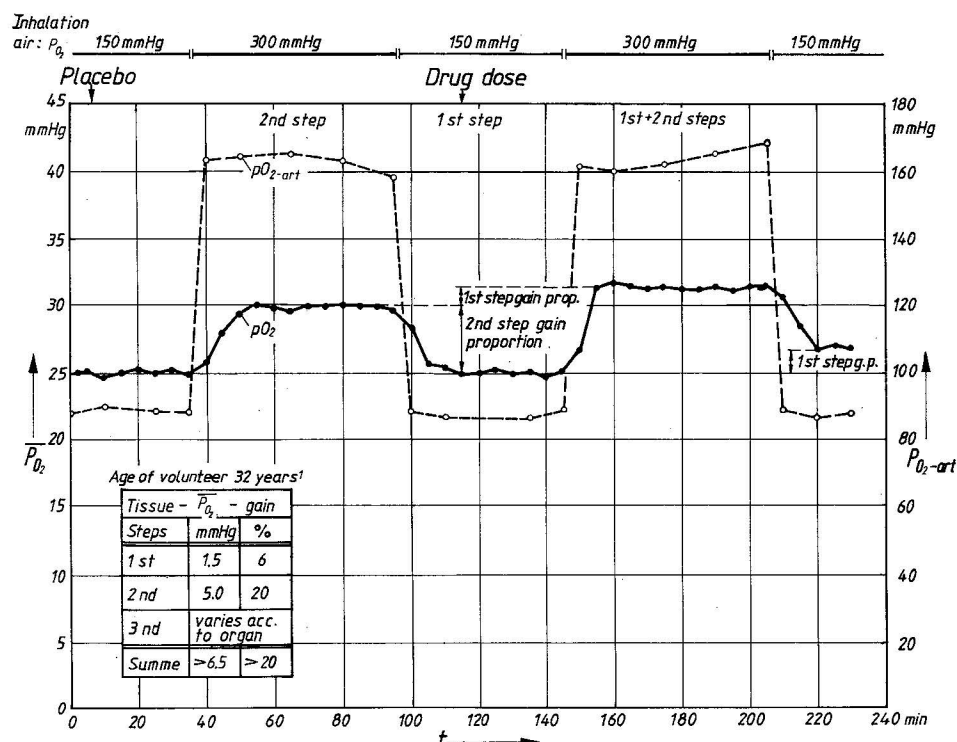


Fig. 158 Using large-area PO_2 electrode for intracutaneous measurement of the mean PO_2 level in the underarm of a person, and measurement of the arterial PO_2 after doubling the PO_2 of the inhalation air alone (2nd step) and after doubling + drug combination dose (1st + 2nd steps). Measurements: H. G. Lippmann

¹ In older age (e.g. $PO_{2-art} = 70-80$ mmHg) the gain in tissue PO_2 is significantly greater! The gain proportion of the 1st step is mainly due to the reduction of the mean venous PO_2 , as in [250]

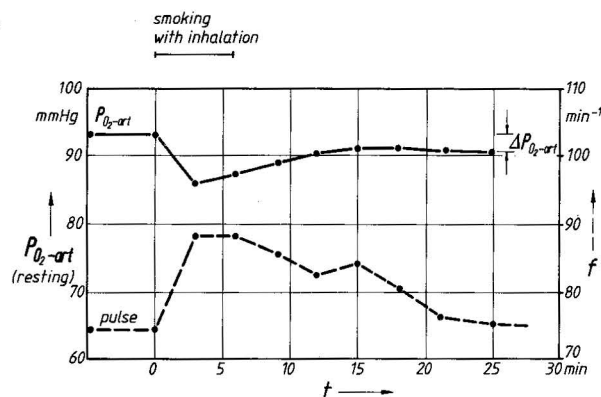


Fig. 159 Influence of smoking a cigarette on the momentary levels of the arterial resting PO_2 and on pulse frequency. Male person, 71 years of age. Experiment to demonstrate the influence of the smoking risk factor on the arterial resting PO_2 . Slight reduction

urement examples given in this book show again and again the astonishing dynamics and reactivity of both PO_2 values. Above all, however, they show that, in health crises of the most varied kinds, *guidelines as to the necessary, appropriate or possible medical action can be derived from the shifts of the arterial and venous oxygen partial pressures, measured under resting conditions.*

The effects of cures of a general kind, of holidays, climatic influences and of a change in lifestyle are reflected in changes of the PO_2 values or in the value of η which follows from them. Thus for example, in the case of a 71-year-old person in whom distress had caused his PO_{2-art} to drop to 78 mmHg (10.4 kPa) a few months after implementation of an O₂MT regeneration

treatment, an increase in PO_{2-art} to 93 mmHg (12.4 kPa) was measured as a *vacation effect* of a 21-day stay by the sea.

Our observation, summarized in Fig. 159, that a marked momentary and a slight lasting drop in the resting PO_{2-art} is caused by *smoking a single cigarette* (with inhalation), must also be mentioned here. This observation provides a new aspect for the designation of chain smoking as a risk factor, for the slight lasting drop in the PO_{2-art} accumulates in chain smoking.

In order for the O₂MT to be of use on a broad basis to the health system, certain technical conditions must be fulfilled in the provision of the oxygen and in the PO_2 measurement technology. The questions connected with these are discussed in the following section.

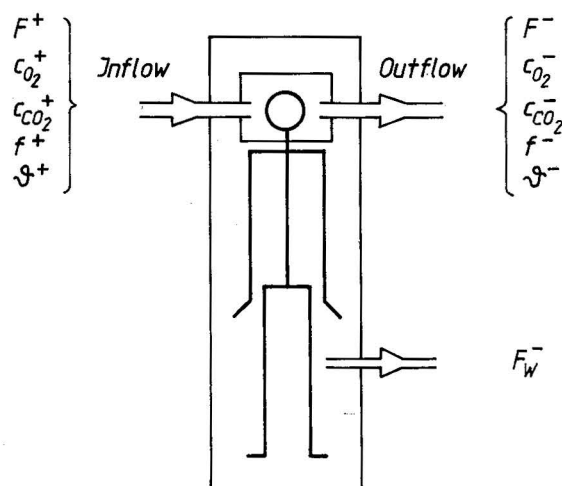
3. Technical foundations

3.1 Technology of the application of air mixtures with increased PO_2

3.1.1 Theoretical aspects

In order to keep the expense and, in particular, the O_2 requirement for the implementation of the O_2 MT as low as possible, the problem in the

O_2 application must be solved in such a way as to allow only a slight O_2 loss. In addition to this, the technical solution must not cause more



	Inflow		Outflow		Normal air (phys.)	
	Symbol	Level	Symbol	Level	Symbol	Level
Total volume flow	F^+	$7-10 \text{ l min}^{-1}$	F^-	$=F^+$	—	—
O_2 -concentration	$c_{O_2}^+$	40%	$c_{O_2}^-$	$\sim 35\%$	$c_{O_2}^*$	21%
CO_2 -concentration	$c_{CO_2}^+$	$\leq 1\%$	$c_{CO_2}^-$	$\sim 5\%$	$c_{CO_2}^*$	$\rightarrow 0$
rel. air humidity	f^+	$\sim f^*$ (or $\sim 80\%$) ¹	f^-	$\sim 95\%$	f^*	40-60%
Temperature	g^+	$\sim g^*$ (or $\sim 37\%$) ¹	g^-	$\sim 37\%$	g^*	18-22°C
Heat flow	—	—	F_w^-	14 kcal/min	—	—

Fig. 160 The significant factors to be considered in the administering of O_2 enriched air

¹ Without warming and moistening of inhalation air in the nose-throat area (e.g. when a nose tube is used). Figures for the 36 h O_2 multistep therapy processes GK 4-I to GK 4-IV

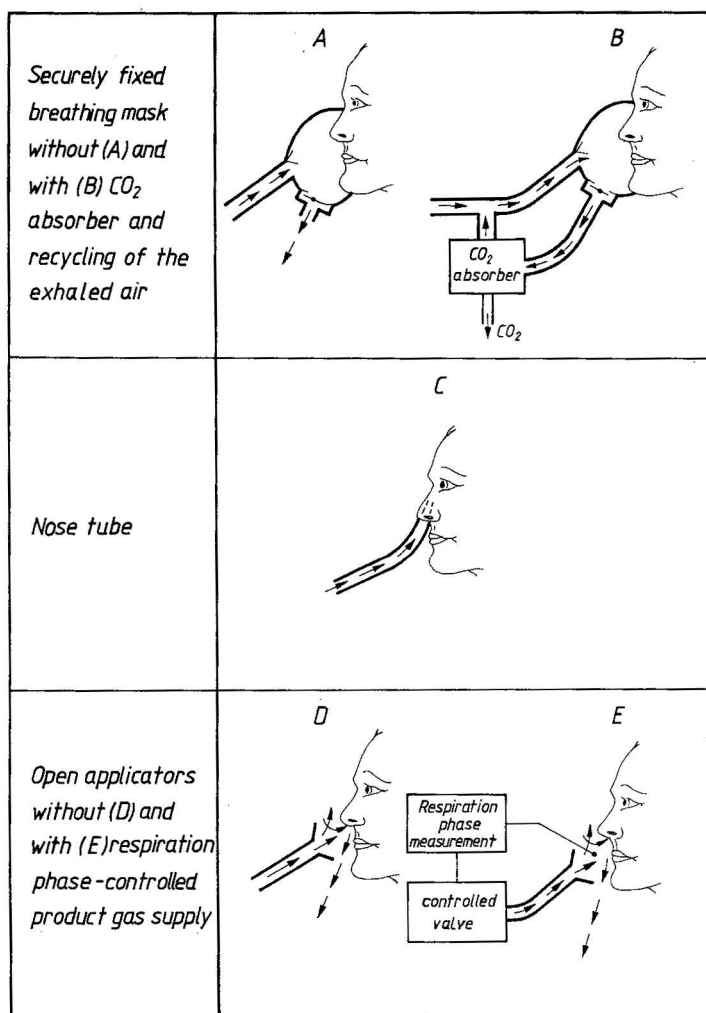


Fig. 161 Various principles in the application of O_2 enriched air

than slight discomfort in sleep, in sedentary work, in the use of a bicycle ergometer or even in reading with glasses. For this optimization it is useful to be aware of the *theoretical foundations of the application of air mixtures with increased P_{O_2}* [5, 279].

The *general application system*, the parameters of which are compiled in Fig. 160, should primarily incorporate a particular flow volume F^+ with a given O_2 concentration $c_{O_2}^+$. Because of special side-effects in the application (e.g. mixing of inhalation and exhaled air, thermal isolation) and in the provision of the O_2 -enriched air, however, it can happen that "environmental conditions" are changed in a way that cannot be overlooked. Quite apart from the primary conditions named, it must also be ensured that the CO_2 concentration $c_{CO_2}^+$,

relative humidity f^+ and temperature ϑ^+ do not exceed certain limits in the inhalation air provided.

The required or tolerated values of these primary and secondary parameters are summarized in Fig. 160, together with those data of the expiration air that are possibly relevant for the quantitative assessment of the expenditure of the process (F^- , $c_{O_2}^-$, $c_{CO_2}^-$, f^- , ϑ^-), and with the heat dissipation of the whole body ($F\bar{w}$), which must also be considered.

The various principles of application are shown in Figs 161 and 162. On the basis of the various clinical methods of administering oxygen, it seems reasonable to use a respiration mask, a nasal cannula or some other specially designed applicator. By contrast to the clinical routine

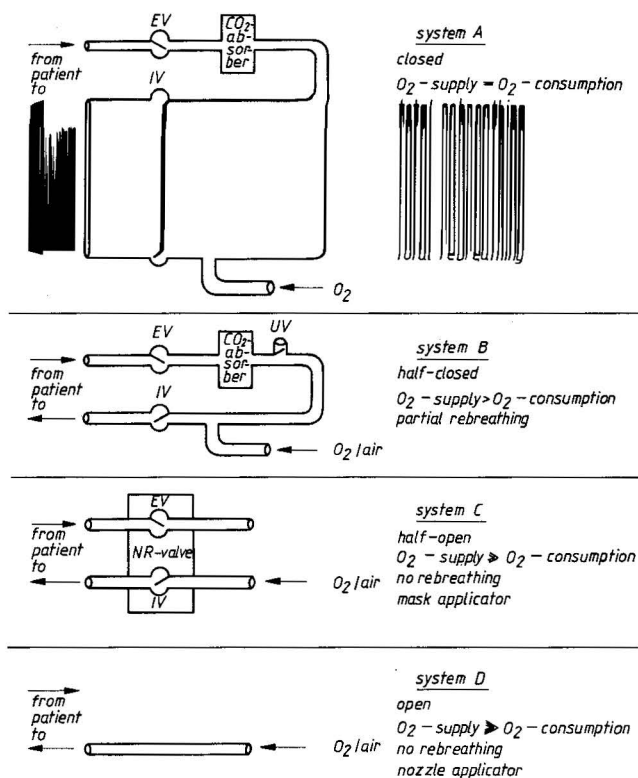


Fig. 162 O₂ application systems (scheme): EV = exhalation valve, IV = inhalation valve, UV = excess valve, NR = non-rebreathing valve (e.g. AMBU, RUBEN)

use of such means, it is of great importance here that the applicator should restrict, hinder or disturb the user's sense of well-being in any other way as little as possible.

As has already been said in Paragraph 1.1.8.6, the rate of lung-conditioned partial non-responders to O₂MT in the 36 h procedure depends very much on the PO_{2-art} , measured at rest and during O₂ inhalation before the start of the treatment. It has been the aim since 1979 to arrange the O₂ application in such a way that $PO_{2-art} > 120-125 \text{ mmHg}$ (16.0–16.7 kPa) is measured during the procedure.

In practice an O₂ nozzle applicator such as the one in Fig. 163 was used until 1982. Using this, *insufflation is performed in the open system*, according to the common anesthesiological definition. With slight modifications (O₂ spectacles, O₂ douches, many types of catheters and applicators), this type of application is also used in other branches of medicine, e.g. *for long-term help in the home in chronic cor pulmonale and respiratory insufficiency*.

Like every other respiratory gas, oxygen can be administered in a closed, half-closed, half-open or open system, as can be seen from Fig. 162.

System A. A respiratory system is *closed*, when the total mixture of expiratory gas is re-breathed. This necessitates CO₂ absorption and an O₂ supply corresponding to the current requirements (< 500 ml/min in adults at rest).

The closed circular system is a practical example, whereas the so-called alternating system is hardly used any more these days.

System B. When a greater quantity of O₂ than the patient consumes is added to the given circulatory system, only a partial re-breathing can occur. The excess respiratory gas arising from this is drawn off through a valve. We call this kind of system *half-closed*.

System C. If the supply of external gas becomes so great that no more re-breathing can occur, we have a *half-open* system. The arrangements are simplified here, as no CO₂ absorption is required. The only remaining functionally necessary task is then the separation of the inhalation from the exhalation gas mixture, and this is undertaken by a non-rebreathing valve (practical models are e.g. Ruben or Ambu, mask applicators with storage balloon).

System D. All systems in which neither the freedom to re-breath nor the supply of respiratory gas is exactly controlled, are termed *open*. The administration of oxygen belongs to this category, when performed with nasal cannulas, insufflation catheters, "oxygen spectacles" or nozzle applicators.

Figure 164 shows and compares the levels of O₂ flow required in order to achieve the same increase in the PO_{2-art} at rest with the four systems of O₂ application. According to this, the open system is a very uneconomical process,

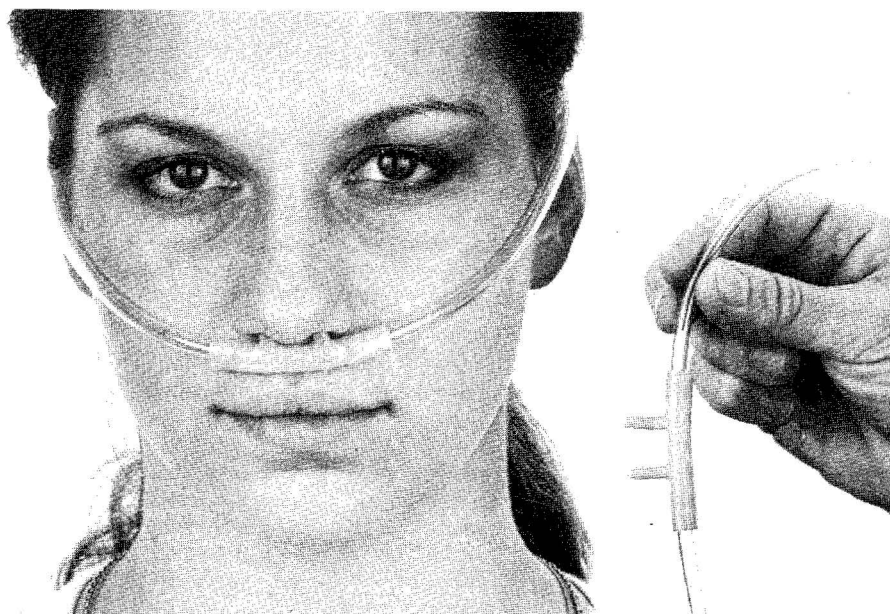


Fig. 163 O_2 nozzle applicator (open system), comfortable for user, therefore much used until 1982 despite great O_2 losses

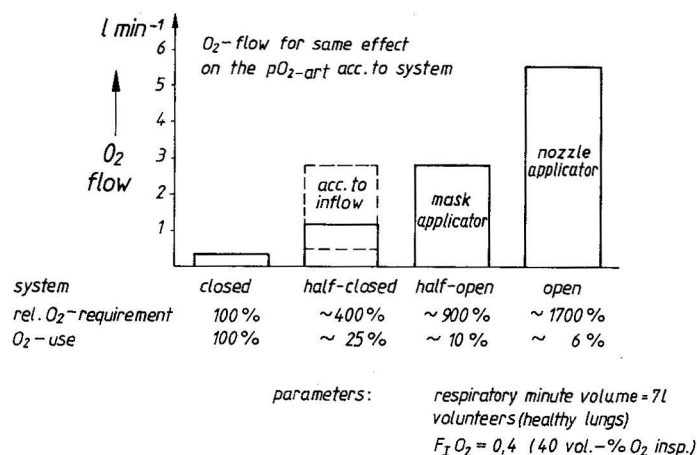


Fig. 164 O_2 flow for the 36 h O_2 O_2 multistep therapy process dependent on applicator system. The characteristic of the new soft plastic mask applicator is between the (previous) mask and nozzle applicator (relative O_2 requirement ~1360%; O_2 use ~8%)

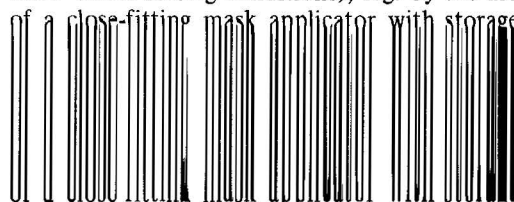
requiring 10–20 times the O_2 flow needed in the closed system. There is a great “therapeutic range” in O_2 application. Therefore suffice it to give two limits, one corresponding to the minimum O_2 supply required for successful therapy, and the other corresponding to the maximum permissible amount (prevention of toxic side-effects in long-term application).

The lower limit in the 36 h O_2 MT variant is a flow that will certainly bring about a P_{O_2-art}

of about 125 mmHg (16.6 kPa), so that the “switching threshold” for this procedure is reached or crossed.

The upper limit for the procedures lasting several hours is an O_2 concentration of 40 vol% O_2 , which is generally accepted to be unproblematical, and which is achieved using a mask applicator with storage balloon with a mean flow of 3.5–4 l/min.

If too great an O_2 flow to the lung is brought about in the 36 h O_2 MT procedure (at a normal RMV under resting conditions), e.g. by the use



of a close-fitting mask applicator with storage balloon, the PO_{2-art} levels of, e.g. 250 mmHg (33 kPa) can result during the treatment. With such excessive levels a gradual counter-regulation in the lung system normally occurs, which in our example reduced the given starting value to 200 mmHg (26 kPa) after 20 min, and to 150 mmHg (20 kPa) after 40 min. It was often

observed that under conditions of the occurrence of such counter-regulation, the lasting increase in PO_{2-art} after the procedure is only of a low level.

In the 15 min O_2 MT quick procedure, in which the PO_{2-art} reaches levels of 350 mmHg (47 kPa) under an O_2 flow of, e.g. 30 l/min, but in which a high RMV exists at the same time and, furthermore, the duration of the individual session is only short, the counter-regulation is insignificant.

3.1.2 Practical aspects. Measurements confirm the O_2 mask applicator with storage balloon to be a good solution

In order to maintain the long-lasting improvement in the O_2 status after O_2 MT, the O_2 flow must be selected in terms of the level and duration so that the "switching threshold" of the procedural variant used (which shows a not inconsiderable individual variation from person to person) is crossed. The fact that in the past some medical experts were repeatedly unable to confirm the lasting improvement in the O_2 status by means of O_2 MT, or were not able to

confirm it with the frequency found elsewhere, was due to this condition not being fulfilled — partly due to ignorance of its existence [17]). The faultless implementation of the O_2 administration is therefore one of the most important tasks in the practice of O_2 MT treatment.

Instead of theoretical considerations of O_2 administration with the mainly used open and half-open systems, which had been made in the

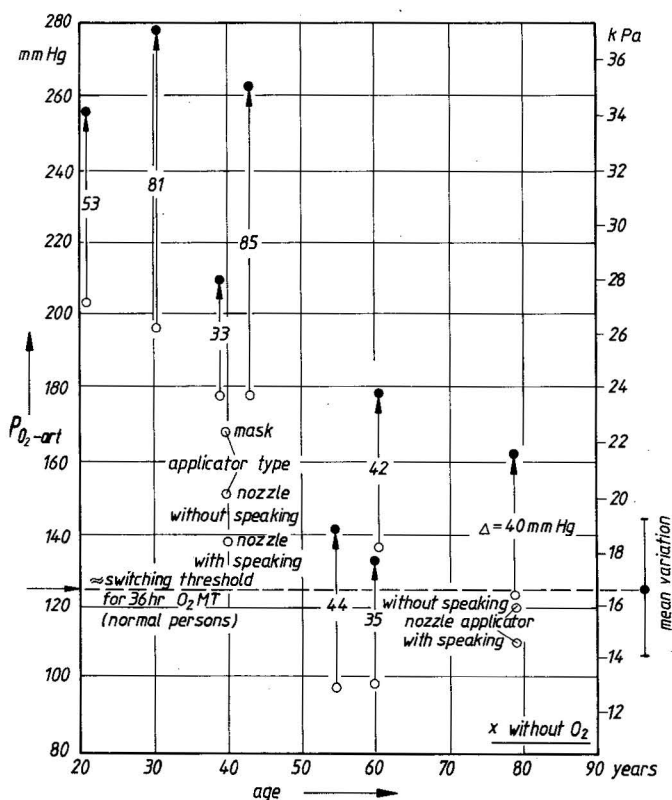


Fig. 165 Measurements of the arterial PO_2 , at rest, under an O_2 flow of 4 l/min through different applicators of soft synthetic material without and with storage balloon. Applicator quality: Mask applicator with storage balloon, very high; mask applicator without storage balloon, high; nozzle applicator, low

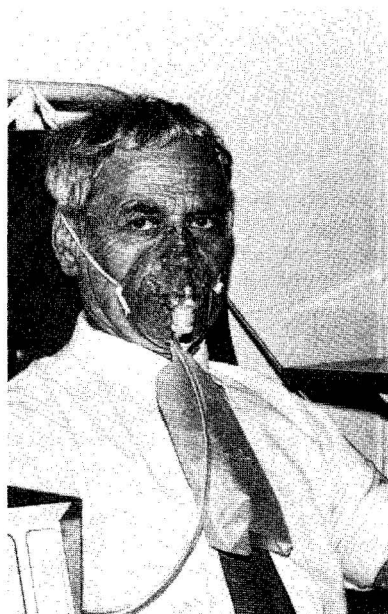


Fig. 166 O_2 mask applicator of soft transparent synthetic material with storage balloon, type MA-SW (half-open system). Most used design; very low O_2 loss; comfortable for the user



Fig. 167 O_2 mask applicator with storage balloon, type MA-SH (half-open system). Somewhat uncomfortable for the user but nevertheless much used in shorter procedures with high O_2 flow

3rd German edition of this book, we want to limit ourselves here to the *assessment, by means of measurement, of the quality of the various applicators used in practice today*. We measured the PO_{2-art} at rest on patients of various ages 20 min after commencement of an O_2 flow of 4 l/min. The results are summarized in Fig. 165.

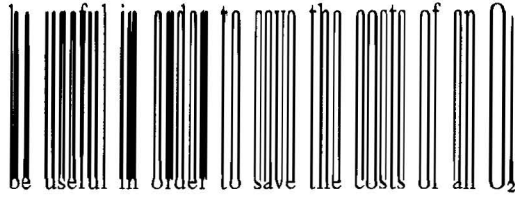
The lowest PO_{2-art} values (not included in the figure for reasons of clarity) were obtained when nasal tubing was used, which is common in intensive care units, for example, and with which the oxygen is administered into one of the nostrils. This type of application, in which there are very high O_2 losses, was considered to be of a "very low standard".

Somewhat higher PO_{2-art} levels were measured using the *nozzle applicator* (Fig. 163), but these were still not always sufficient for the crossing

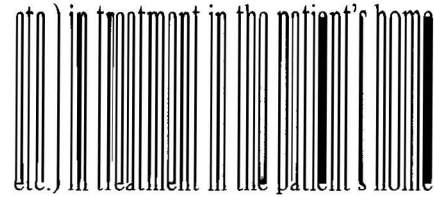
of the switching threshold of the 36 h O_2 MT procedure. Furthermore, these levels dropped considerably if the person spoke and thereby changed from respiration through the nose to respiration through the mouth. Better values were achieved with the *mask applicator*, with which the oxygen administered is still fully effective even when respiration occurs through the mouth.

The *mask applicator with storage balloon*, as shown in Figs 166 and 167, gave by far the best results. The economic nature of this type of applicator, in terms of O_2 , rests on the fact that even the oxygen which is administered during the expiration phase is led to the lung with only very little loss. The process of the inflation and deflation of the storage balloon can be used to *adapt the intensity of the O_2 flow to the respiratory minute volume*. The adaptation has

been accomplished when, at the end of the inhalation phase, the storage balloon has just been deflated. This simplifying procedure can



flowmeter or the expensive technical equipment for physical exertion (bicycle ergometer, manual ergometer, rowing device, running belt



3.1.3 Administration of oxygen in a closed room

The O_2 enrichment of the air of a whole rest room, in accordance with the variants shown in Fig. 168, relieves the user of the necessity of wearing a more or less uncomfortable applicator. This significant advantage is opposed by several disadvantages, some of them serious: an augmented proportion of O_2 in the air in the vicinity of flammable objects means an increased risk of fire. The O_2 enrichment of the air of a whole room (Fig. 168 A) therefore demands a series of safety measures of unquestionable efficacy, the expense of which prohibits a broad application of this system from the start. Only relatively small working cabins or resting tents (Figs 168 B and C), in which the risk of fire is reduced due to a smaller volume, can be used in such a way as to fulfil fire precautions and aid the necessary measures within reasonable limits.

The required total amount Q_K of O_2 -enriched air for maintaining an atmosphere having a constant oxygen content cO_2 in a cabin with the volume Q_0 is composed of the

- flow of the feed-gas (F_{KA}) with the oxygen concentration cO_{2KA} and the

- initial filling volume to attain the desired oxygen level in the cabin by “rinsing” and “blowing”.

Provided that the CO_2 is not absorbed by special devices, the requirements of O_2 -enriched air during a treatment are primarily determined by the fact that, at the end of the session, the CO_2 concentration of the recycled air must not exceed the limit of $\leq 1\%$ despite the continuous generation by the experimental subject ($\approx 5\%$ CO_2 in the expiration air). The diagrams in Fig. 169 give detailed information on the volume of O_2 -enriched air thus required and also for the initial filling of the cabin. It can be seen that, for longer periods of administration, the amount of O_2 -enriched air fed into the cabin must be approximately 4 (!) times greater than the volume needed by the individual because of the necessary removal of CO_2 . On the other hand, short periods of application are uneconomical from the start, due to the large initial volumes for “charging” the treatment chambers, cabins or whatever.

An improvement of this unfavorable, O_2 -wasting procedure could be attained by the reduc-

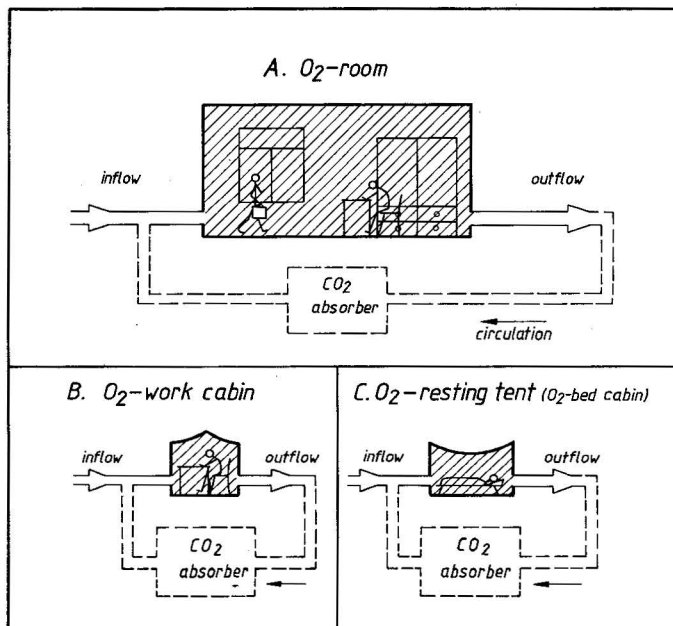


Fig. 168 The application of O_2 -enriched air in rooms for different purposes

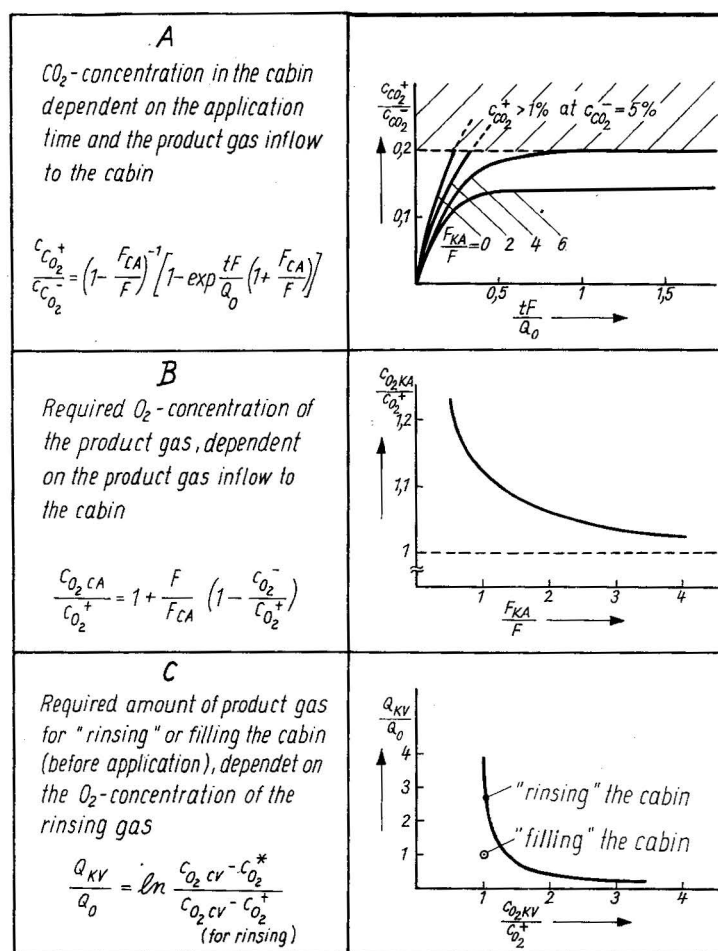


Fig. 169 The requirement for O_2 -enriched air (product gas) for the operation of a cabin

tion of the CO_2 content of the cabin atmosphere by means of measures that do not consume O_2 . However, because such means demand relatively complicated technology (elimination of CO_2 through selectively permeable membranes) or a high level of servicing (CO_2 elimination by chemical absorbers), they are not very suited to the applications under consideration in this book.

In addition to the proportions of O_2 and CO_2 , the temperature and humidity in the cabin must also be compulsorily regulated within the given tolerance margins (cf. Fig. 160). The maintenance of a given cabin temperature requires the (relatively high) heat production $F\bar{w}$ to be compensated for by a respective heat dissipation from the inside to the surroundings

of the cabin. The proportion accomplished by convection (with the O_2 /air stream) is certainly very slight here ($\leq 10\%$). A consistent heat balance must be achieved mainly by a sufficiently good heat conduction via the cabin wall and/or by special cooling systems.

The humidity of the cabin atmosphere can be down-regulated to a physiologically favorable or at least tolerable level by a suitably adjusted humidity of the O_2 -enriched feed-gas, the production of which is necessarily connected with a more or less appreciable dehumidification of the "product gas". Increasing the humidity of a gas does not pose any difficulties. This method is only really of practical significance for the care of infants.



Fig. 170 Respiration mask, worn over the mouth and nose, with warmth-isolating terry-cloth cover for use in the O_2 multistep sauna. Construction type: Oxyparat Allihn, D-8000 Munich, FRG

3.1.4 Oxygen application for special conditions

O_2 applicators for use in the O_2 MT sauna had to be developed bearing the high room temperatures in mind. Figures 170 and 171 show constructions with which burns due to contact with hot metallic parts etc. can be avoided.

With the construction shown in Fig. 171 an O_2 -enriched zone is formed in front of the nose and mouth, from which the person breathes the desired gas mixture.

In order to keep O_2 losses at a low level, it is not only necessary to optimize, as discussed the O_2 inlet as such, but also to adapt the supply of O_2 to the respiratory process itself. Theoretically, there is a slight loss of this type if the O_2 supply only occurs in the immediate phase of inhalation, when a high rate of influx exists. Measurements using impedance plethysmography, as in Fig. 172, showed that the favor-

able interval of the respiration phase amounts to roughly 30% of the total time needed for inhalation and exhalation (duration of respiratory period).

Respiratory phase switches, controlled electronically by a thermistor, have not yet been able to take the place of the much simpler *O_2 -saving storage balloon*. They were complicated and expensive. The respiratory phase switch, controlled *thermally* by the respiratory gas flow, is much simpler in its design and effect and is, in the design shown in Fig. 173, combined with the O_2 mask applicator. This kit was put on the market early in 1986 by Allihn, Munich, FRG. There is a 50% saving of oxygen compared with the mask applicator without storage balloon.

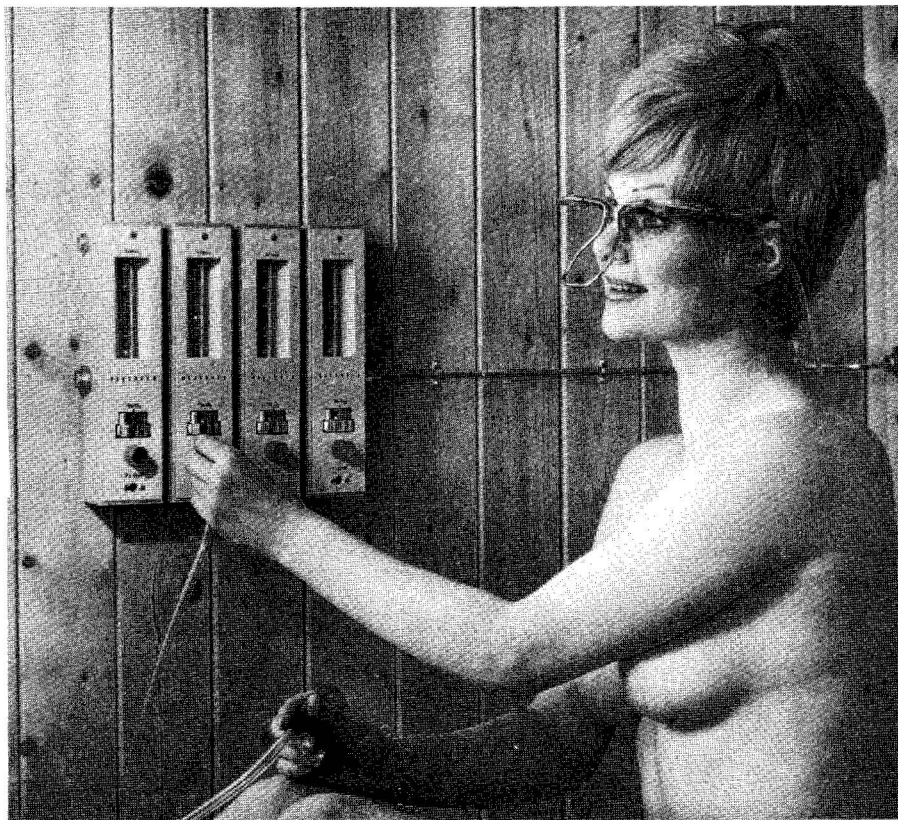


Fig. 171 O_2 applicator in spectacle form for sauna visitors (OXYTHERA). The control unit allows individual dosage of oxygen from pressure cylinders (flow rate and O_2 content of the breathed gas mixture). According to the number of sauna visitors, any number of these units can be coupled next to one another. Design: H. G. Lippmann, construction type: Manfred von Ardenne Research Institute, Dresden, GDR

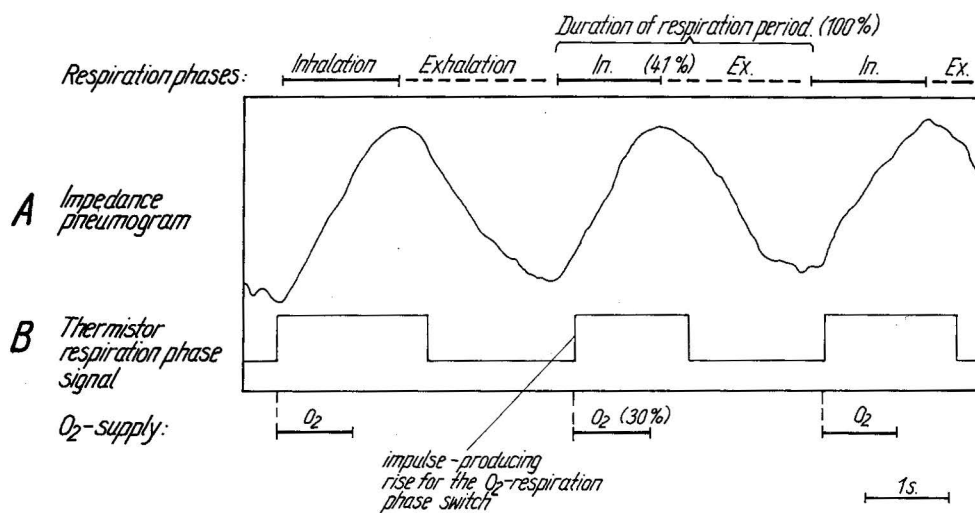


Fig. 172 Respiration phase measurements in resting conditions, with impedance plethysmography (A) and the oscillogram of the thermistor unit (B). Its signals control the go/no-go rhythm of a valve which releases 30% oxygen only in the early inspiration phase

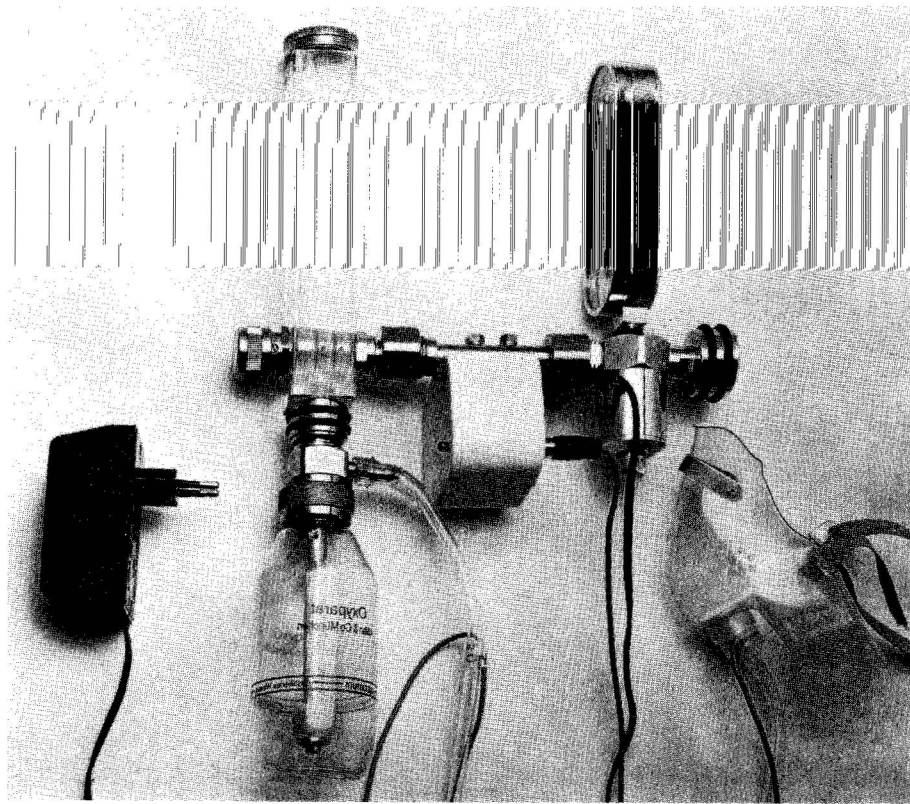


Fig. 173 Respiratory phase switch, thermo-controlled by the respiratory gas flow (Manufacturer: Allihn & Co., D-8000 Munich 70, FRG)

3.1.5 Hyperbaric oxygen therapy and hyperbaric O₂MT. Most intensive variants

The oxygen therapy using a hyperbaric chamber [274, 275] and the O₂MT do not oppose each other; rather, they should be seen as variants closely bound together and complementing each other. This complementation refers mainly to important fields of application where the higher O₂ pressure brings about greater or faster effects, which do not occur in the normobaric O₂MT (e.g. combat of anaerobic infections such as gas gangraene, tetanus, or treatment of acute hearing loss etc.). From the point of view of O₂MT it virtually goes without saying that in treatment in the hyperbaric O₂ chamber the discovered capillary wall switching mechanism of the blood microcirculation (see Paragraph 1.1.1) is often, or even usually, triggered in a positive direction which lastingly improves the O₂ status. The occurrence of this "high-charging" and thereby existence of a real methodological relationship are also made probably by the fact that the same indications are given for the hyperbaric oxygen therapy (with the exceptions named), as were derived from the results of many tens of thousands of treatments with O₂MT. The following indications for hyperbaric oxygen treatments were given as early as 1968 [274, 275, 275a]:

Neurology:

Stroke and its late effects
Prognosis of a successful, extracranial bypass operation
Cerebral circulatory disorders

ENT:

Sudden loss of hearing
Tinnitus

Surgery, angiology:

Chronic ulcera cruris
Skin transplantation
Arteriovenous occlusive disease

Further indications:

Multiple sclerosis
Spinal cord injury
CO poisoning
Cyanide poisoning
Ergot poisoning
Osteoradionecrosis
Chronic osteomyelitis
Crush injury
Compression syndrome
Actinomycosis
Burns
Cerebral hypoxia after attempted suicide by strangulation

Therapy-resistant ventricular and duodenal ulcers
 Malignant otitis externa
 Hardness of hearing due to noise
 Peripheral circulatory disorders

The extent of the increase in the resting PO_{2-ven} during the different treatment variants with hyperbaric oxygen has not yet been investigated. There is also a lack of published results on the lasting improvements in the O_2 status after treatment. Since very high levels of the PO_{2-art} (850–1140 mmHg, corresponding to 113–152 kPa) were detected during hyperbaric oxygen treatments [276], we can be sure that, in accordance with Fig. 3, PO_2 levels ≥ 50 mmHg (8 kPa) exist at the venous end of the capillaries without physical exertion. With the named PO_2 pressures and the usual management, with, e.g. 20 sessions of 90 min duration in the chamber, the triggering of the switching process must occur as in the 36 h O_2MT procedure (without significant physical exertion), and thus also the long-lasting effect. In order to *intensify the effects of the hyperbaric oxygen therapy* it is obvious that the 1st and the 3rd step of the O_2MT should also be applied. This thought leads us to the interesting concept of the *hyperbaric oxygen multistep therapy* with additional increase of the PO_{2-ven} under O_2 excess by means of raising the capillary blood flow $\dot{Q}$ by strong physical exertion. The reader should remember here the relation to the strength of the effect of the O_2MT procedures, shown in Paragraph 1.1.1.2. In treatments in the high-pressure chamber, too, this measure for the raising of the PO_{2-ven} during the treatment (by means of physical exertion) should not be omitted if at all possible (increase in the effect and reduction in duration of the procedure). A scientific investigation into the specific effects of the hyperbaric oxygen multistep therapy is at present being carried out by B. Fischer (see below).

The effort involved in the hyperbaric oxygen multistep therapy is unquestionably justified in the treatment of particularly severe cases and in cases in which an additional pharmacodynamic effect of the oxygen should be exploited ($PO_{2-art} > 100$ mmHg $\triangleq$ 130 kPa).

Peripheral circulatory disorders of the lower extremities in diabetics, which have reached the stage where amputation is becoming necessary, are an example of this. In such situations we must use all means to combat the peripheral circulatory disorders. In the normobaric O_2MT we had therefore recommended the inclusion of the HOT* treatment and, if necessary, hemodilution in such cases [74]. The chances of

success seem much better even than this using the hyperbaric oxygen multistep therapy, if necessary again with the further complementary steps of HOT* and hemodilution. For both hyperbaric and normobaric O_2MT a normal hematocrit is an absolute prerequisite. If it is higher than normal, it should be reduced to at least 45 %. A study of therapeutic limits of such intensive variants should soon be carried out with patients who have reached the critical stage discussed.

Recently the term HBO (hyperbaric oxygenation) has been used increasingly and internationally for hyperbaric medicine, and in many countries there are numerous systems for it, starting from one-person chambers up to large high-pressure chambers for the simultaneous treatment of several persons (up to ten patients and more) at pressures up to 10 bar and more ($\triangleq$ 1 MPa).

An exemplary high-pressure chamber has been in use in the Fachklinik Klausenbach für Frühgeriatrie der LVA in Nordrach-Klausenbach, FRG, since the early 80s. Senior Consultant Prof. Dr B. Fischer has performed well over 10 000 treatments without complications and has gained particularly good results in the combat of diseases of the inner ear (sudden loss of hearing, deafness due to explosions etc.) and in the treatment of cerebral insufficiencies. An exchange of experiences has been going on for a good year.

It has been internationally shown in the last few years that, with various indications, it is possible to perform therapy more advantageously using lower pressures than had been seen from the experiences of submarine medicine.

We would particularly refer the reader to the papers by Holbach, Caroli and Wassmann [277], in which it was shown that better neurological results were attained at an excess pressure of 0.5 bar (50 kPa) than at double the level.

Lower levels of high pressure make possible a simpler type of construction for the chambers, and it is even possible to use these simpler systems mobilely. Erwin Braun in Engelberg, Switzerland, designed and produced a mobile high-pressure chamber with a maximum operational pressure of 1.25 bar (125 kPa), in which up to nine persons at a time can sit and undergo therapy. Figure 174 shows a side view of this mobile system, presented in Basle in February 1986, and also shows how a running-belt is mounted in this chamber to enable precise ergometry, on which a volunteer exercises, connected to the O_2 supply.

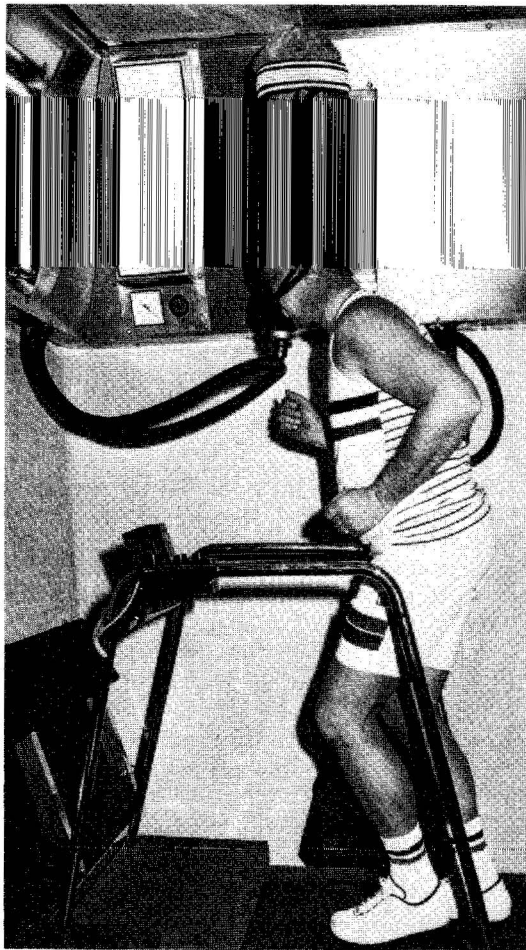
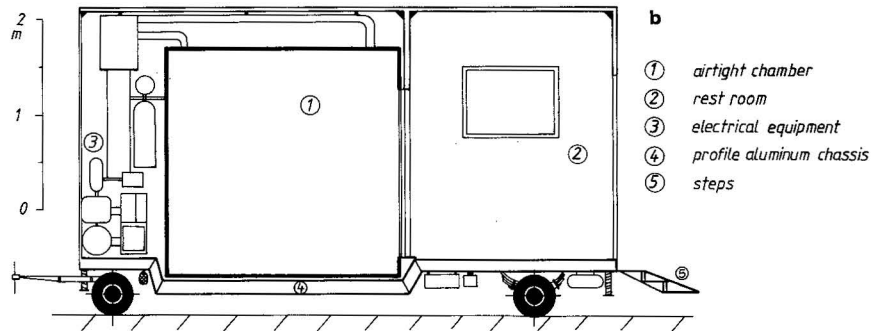


Fig. 174 Mobile hyperbaric O_2 chamber (up to 1.25 bar) according to Erwin Braun, Engelberg, Switzerland. Inside view

a) Inside view with running belt for exertion
b) Scheme of layout



The development of mobile high-pressure chambers of this type makes possible the necessary extension of the basis for clinical research with HBO, and we regard this as being so important that we have ordered one of the first chambers of this type and want to make it available to the external branch of our Institute at the nearby Weisser Hirsch clinic.

It should also be noted that the pressure-equivalent "effective diving depth" lies at 10 m and below. That means that the "zero time" lies in the normal therapeutic times and that it is always possible "to surface" at short notice. There is no longer any need for a decompression department.

3.2 Technology of the provision of air mixtures with increased P_{O_2}

3.2.1 Oxygen requirements in the various procedures of the O_2MT

The additional O_2 requirements of the organism under the various variants of the O_2MT at physical rest and in physical exertion is a decisive value for the calculation of the systems for O_2 provision necessary for therapy. This value determines the *time of provision* for oxygen from a store (pressure cylinders, Dewar vessels with liquid oxygen), and in devices for continual O_2 supply it determines the *dimensions of the O_2 production performance* of the device.

The values of the *oxygen flow rates $\dot{Q}_{O_2}$ in the most important procedures of the O_2MT* are to be taken from Fig. 175. In the interests of a good procedural effect, it must always be ensured that a *flow rate of the respiratory gas*

$Q = \dot{Q}_{O_2} + \dot{Q}_{N_2}$ is adaptable of the prevailing level of the respiratory minute volume (RMV). For the adjustment and control of the supply of respiratory gas or additional O_2 to the applicator, gas flow meters (rotameter principle, cf. Fig. 171, left, or with analogue display) with different measuring ranges are necessary. These flowmeters are often combined with an additional fine valve and also with a gas humidifier.

In the O_2MT quick procedure (variant GK 2), in which the RMV is multiplied as a result of the high level of physical exercise, the O_2 flow rate is also multiplied, as can be seen from Fig. 175. Although the 15 min O_2MT quick procedure works with virtually pure oxygen,

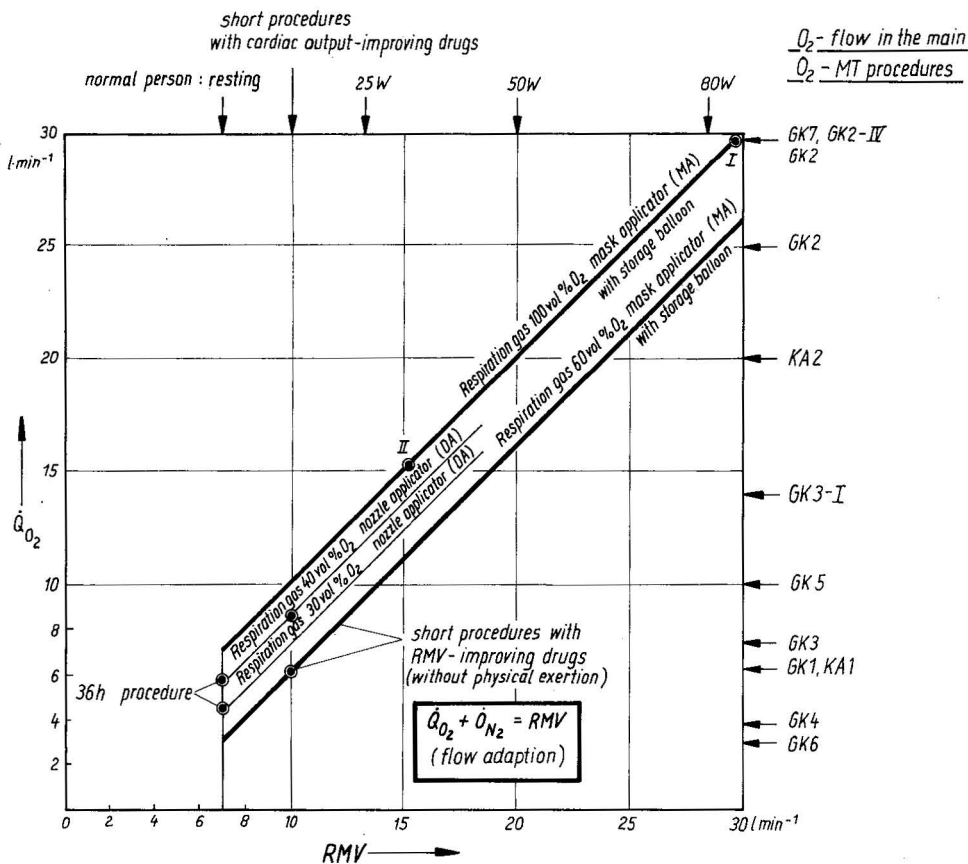


Fig. 175 Oxygen flow rate $\dot{Q}_{O_2}$ in the main O_2MT procedures. Mask applicator with storage balloon (semi-open system)

and although the flow rate for this variant is between 25 and 30 l/min, the O₂ requirement for the whole procedure is reduced to roughly

5–10% of that for the 36 h procedure because

the duration of the quick procedure is only 1–3 x 15 min.

For non-able-bodied or disabled persons, for whom it is not possible to raise the cardiac output by physical exertion, we tried to reduce the

duration of the procedure by the administra-

tion of drugs, which increase the cardiac output and RMV for some hours, even at physical rest.

Table 18 O₂ supply from stores [279–284]

Method	Work principle	O ₂ content	Content (volume)	O ₂ supply output l/min	supply volume (normobaric)	Area of use	References (remarks)
1 Pressure cylinders	1.1 Filled in special works for technical gases (transportation increasingly awkward above 20 l cylinders)	≈ 99	0.8 l	variable	160 l	outpatient	steel light weight cylinder (200 at) in carrying bag 280
			2 l	dto.	400 l	also outpatient	
			10 l	dto.	2000 l	at home	
			20 l 40 l	dto. dto.	3000 l 6000 l	stationary central supply units	
2 Central supply units	2.1 Supply at reduced pressure from batteries of 40 pressure cylinders (laborious)	≈ 99 (pressure in pipe 5 at)	larger number 40 l cylind. e.g. 2·10	4–16 per single delivery	60 000 l in use in reserve	in larger clinics central supply units	278, 280 (centre conveniently located)
	2.2 Supply from liquid oxygen, using a transportable cryo-tank with e.g. 100 l contents (pressurized gas producer)	≈ 99 (pressure in pipe 5 at)	several tanks (10 ⁴ l liquid O ₂)	4–16 per single delivery	80 000 l per tank, storage time 85 hrs (8·10 ⁶ l)	in larger clinics central supply units	280, 281 Linde AG, Tech. gases, D-8023 Höllriegelskreuth (care in the handling of liquid oxygen) 282
3. Generation by decomposition of oxygen-rich chemicals	3.1 Reaction: $\text{NaClO}_3 + \text{Fe} \rightarrow \text{NaCl} + \text{FeO} + \text{O}_2$	60	equipment mass 2.5 kg (0.88 kg NaClO ₃)	3	180 (2x90) two charges	outpatient very easy to transport	283 Med-ox-equipment from Scott-Aviation, Lancaster, N.Y., USA (two charges, which can be discharged in sequence or parallel)
	3.2 Reaction: $2\text{H}_2\text{O}_2 \rightarrow 2\text{H}_2\text{O} + \text{O}_2$ (catalyst) H ₂ O ₂ as 30% aqueous solution; Perhydrol)	99	(2 kg Perhydrol)	3	200	outpatient	284 (Japanese small-sized equipment 1970)
	3.3 Reaction: $2\text{Na}_2\text{O}_2 \rightarrow 2\text{Na}_2\text{O} + \text{O}_2$ (catalyst or heat)	99	(2 kg Na ₂ O ₂)	3	285	outpatient	284
	3.4 Decomposition, e.g. of KMnO ₄ at T > 200 °C	99	(1 kg KMnO ₄)	3 (after heating-up time)	142	outpatient	283 (mains-operated heating)

3.2.2 The various types of oxygen provision

The technology for the *provision of additional oxygen* at rates of 1.5–5 l/min for a few or for many hours, or at rates of 5–50 l/min for durations of a few hours to a few tens of minutes, has entered a new phase. The most recent developments in the various branches of this specialist technology all have the common characteristic that the O_2 can be delivered to the sick or healthy person in a much more comfortable way than ever before [278]. The needs of patients with certain lung disease, and of asthmatics, can be seen to have contributed just as much to this development as the effort periodically to counteract the increasing air pollution in conurbations of cities. For the O_2 MT this development leads to the fulfilment of the essential technical preconditions in order to enable this therapy to be applied on a broader basis even in smaller clinics, outpatient clinics, medical practices, sanatoria, as well as in the home.

In the systems for *O_2 provision from stores*, summarized in Table 18, *lightweight steel cylinders with a capacity of 160–400 l O_2* can be seen to be advancing in the field of individual requirements. For outpatient application, the production of units with a capacity of between approximately 150 and 300 l has been started, in which O_2 is generated by the decomposition of oxygen-rich chemicals.

In central O_2 supply, the *provision from batteries of 40 l pressure cylinders* (e.g. from Allihn, Munich, FRG, or Weinmann, Hamburg, FRG) and from *liquid oxygen tanks or pressurized gas producers* is being accomplished in larger clinics [282]; cf. especially the production programmes of Linde, Höllriegelskreuth, FRG.

In the system for *O_2 provision from continual production*, which is summarized in Tables 19 and 20, very recent technical developments have caused a new situation to arise. Until now there were virtually only the extensive systems of cryogenic engineering [280, 281] to produce liquid oxygen. The relatively high production performance of systems which are so extravagant in terms of equipment and servicing, limits their application to the direct or indirect supply of large clinics. With the creation of sys-

tems for *O_2 separation with zeolite molecular sieves* [285, 286], *a relative easy provision of O_2 is opened up for application in the home*. A new branch of the medical industry could be in the making. Even *O_2 separation with membrane systems* [287], which is still at a very stage, has already led to experimental set-ups with interesting features [288], cf. Table 20, column 2.1.

It is a fascinating aim of further research on the theme of this book so to develop further the membrane systems for selective gas permeation, that the pressure difference occurring in normal breathing is enough to cause sufficient O_2 provision. Elements which could be helpful in the development of highly selective membranes (under investigation) are indicated in column 2.3 in Table 20 [289]. In the performance of this task a type of O_2 mask would result which would be able to help patients with critically reduced cardiopulmonary performance, up to the total duration of the daily cycle. That such an O_2 mask, which with a light construction could be conveniently carried with the patient in a shoulder bag, could, for example, in persons with advanced lung insufficiency (for whom the O_2 MT does not usually work), permanently produce the same strength of O_2 supply to their tissue as existed in younger years is a thought that spurs us on to intensive action.

In the course of our continuous efforts since 1969 to discover technically and economically practicable methods of O_2 provision with rates between 1.5 and 10 l/min, models were built, or experimental investigations performed into the generation of O_2 by *electrolysis of water*, by *oxygen ionic conduction in solid state electrolytes*, by the *reversible complexing of O_2 to an desorption from organic Co-complexes (salcomin)*, by utilizing *the different gas solubilities in liquids*, and by means of *green algae*. These studies form the basis of the data and assessments given in Table 20. None of these five methods has as yet led to more favorable results than O_2 separation with zeolite systems (and with membranes). For this reason we only deal with the technical realization of these two main methods later in this chapter.

Table 19 O₂ provision from continuous production, zeolite systems [285–288], prospective solution

Method	Working principle		O ₂ concentration vol. %	Size h, w, d (cm) Mass (kg)	O ₂ provision O ₂ addition (l/min)	O ₂ mix l/min	Area of use	Remarks
Separation by zeolite systems	Selective adsorption of N ₂ to specific zeolites	1.1 Pressure swing at excess pressure (250 kPa)	55 to 93	75x30x75 60	4.3 4.85 5.16 4.55	10 (55 vol.%) 8 (69 vol.%) 6 (89 vol.%) 5 (93 vol.%)	at home, in clinics with- out central O ₂ supply, for O ₂ MT variants GK4, GK6; mobile unit on castors, noise level 48 dBA, N=0.4 kW	O ₂ selector a _____ and addition- al reservoirs Development _____ IvA, Dresden, GD _____ R Performance _____ adapted
		2-step cycle			—	—		
		1.1.1 Additional O ₂ reservoir 1	93	0.5 m ³	Storage 450 l (standard)		additional unit at 1.1 for quick procedure GK2, GK2-II, GK2-III	performance _____ adapted to all O ₂ MT _____ variants
		1.1.2 Additional O ₂ reservoir 2	93		Storage 3500 l (special supplement)		additional unit at 1.1 for 120—60 min obstetrics procedure GK2-IV	large series p _____ oduction Hauni-Werke _____ Körber, Hamburg, FF _____ G (1986)
		1.3 Pressure swing at excess pressure	60 to 92	72x30x57 37	2.0 2.3 1.8	4 (60 vol.%) 3 (80 vol.%) 2 (92 vol.%)	at home for long-term therapy with low O ₂ flow mobile unit on castors, noise level 50 dBA, N) 0.28 kW	Permax development _____ and pro- duction Dräg _____ er-Werk, Lübeck, FR _____ (1982)
		2-step cycle						
		1.4 Pressure swing at excess pressure	60 to 95	58x44x41 38	2.0 2.3 1.9	4 (60 vol.%) 3 (80 vol.%) 2 (95 vol.%)	at home for long-term therapy with low O ₂ flow mobile unit N) 0.28 kW	"Oxymat" development _____ and pro- duction Weir _____ mann, Hamburg, FF _____ G (1985)
		2-step cycle						
		1.5 Pressure swing at excess pressure	60 to 96	71x53x37 44.5	3.0 2.6 1.9 1.0	4 (80 vol.%) 3 (89 vol.%) 2 (94 vol.%) 1 (96 vol.%)	at home for long-term therapy with low O ₂ flow mobile unit on castors, noise level 45 dBA, N = 0.35 kW	"Med-O ₂ " development _____ and pro- duction Bud _____ erus, Wetzlar, FR _____ (1985)
		2-step cycle						
		1.6 Pressure swing at excess pressure	60 to 90	adapted to local conditions	200 — 100	400 (60 vol.%) — 120 (90 vol.%)	larger cure centers, smaller clinics, intensive care	large O ₂ sele- _____ ctor, development _____ IvA, Dresden, GD _____ R (1984)
		2-step cycle						

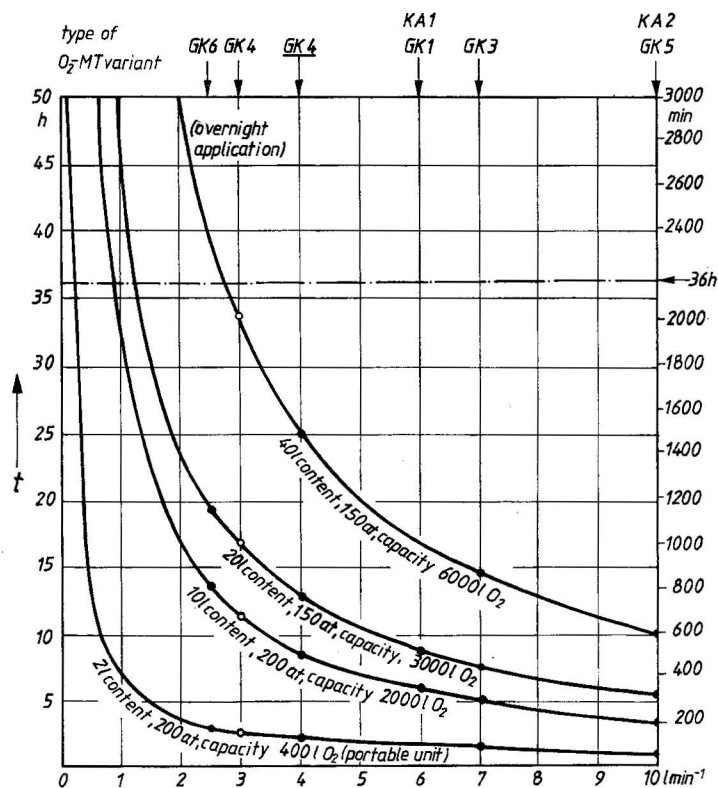


Fig. 176 O_2 delivery capacity of various standard-sized O_2 pressure cylinders expressed as the time t during which a certain O_2 flow Q_{O_2} can be maintained. On the upper abscissa the O_2 demand of some O_2 MT variants is indicated

3.2.3 Oxygen provision from pressure cylinders

The volume and capacity of the various standard types of O_2 pressure cylinders have already been given (cf. Table 18). With the development of the O_2 MT quick procedure and the O_2 MT short procedure, O_2 provision from pressure cylinders has gained importance for two reasons:

1. because the total amount of O_2 required per procedure has become much smaller, compared with the 36 h O_2 MT variant, and
2. because the higher O_2 flow rate necessary for the new short versions of the O_2 MT still exceeds the separation efficiency of the zeolite selectors available at present.

For how long one can manage on a certain type of oxygen cylinders in dependence on the flow rates needed for the common O_2 MT procedures is to be taken from Figs 176 and 177. For the requirement of the 15 min O_2 MT procedure the contents of 2 l bottles are sufficient, as can be seen, for which a convenient portable unit is available. For outpatient use, the contents of one 2 l light-weight steel cylinder, which can be

easily transported in a carrier bag, are often enough.

As soon as we are no longer dealing with individuals, but with larger numbers of patients, the use of large, difficult-to-transport pressure cylinders cannot be avoided. In cure institutions it has proved worthwhile to install a row of 40 l cylinders (filling pressure 150 at, 6000 l O_2 capacity per cylinder), with pressure-reducing valve and in observation of safety regulations, in a fixed position immediately next to access for lorries. From this place the oxygen is led to the individual treatment rooms with their O_2 taps via low-pressure pipes. Each O_2 unit combines a Rossignol valve, an O_2 flowmeter (e.g. rotameter), an air humidifier and a mask applicator of flexible plastic material.

Complete sets of this type can be obtained from e.g. MLW (Leipzig, GDR), EMC (Aachen, FRG), Allihn (Munich, FRG), Eumatron (Munich, FRG), Weinmann (Hamburg, FRG), SMT-Geräte-Vertrieb (Berlin West), Linde (Höll-

Table 20 O₂ provision from continuous production, further systems [287–294]. Recent data on separation of gases by membrane systems are given in Fig. 1

Method	Working principle	O ₂ concentration vol. %	Size	O ₂ provision O ₂ additional l/min	O ₂ mix l/min	Area of use	Literature (remarks)
2 Separation with membrane systems	selective O ₂ permeation by means of membrane systems under difference pressure	2.1 silicon membrane, 50 nm thick, placed on a microporous support	33 (separation factor 2.2)	height ≈ 80 cm width ≈ 110 cm depth ≈ 60 cm	1.5	10 (33 vol.%) membrane surface 400 cm ²	at home for one person stationary unit Development General Electric, Schenectady, New York, USA (1976)
		2.2 polycarbonate membrane, 50 nm thick, placed on a microporous support	4.6 (separation factor 4.8)	something like 2.1	1.5	membrane surface 10 ⁴ cm	at home for one person 1 part granulate PC dissolved in a mixture of 99 parts methyl chloride 0.1 part cedarwood oil and 50 parts trichloroethylene, membrane production by spreading this solution followed by evaporation hollow-fibre bundles, sealed at the ends, still at research state
		2.3 polycarbonate hollow-fibre membrane systems (large surface requiring little space)	46 to 51	small instrument or O ₂ mask	according to membrane surface (and breathing frequency)		at home, at work, also when position changes portable unit
3 Separation by electrolysis	3.1 H ₂ O decomposition (3 electrolysis cells, current density j = 1500 A/m ²)	99 (0.8 mg NaOH per 8 h, filter)	height 143 cm width 73 cm depth 68 cm		—	at home stationary unit 200 kg power consumption 1.8 kW no use	O ₂ equipment Development IvA, Dresden, GDR (1971)
	3.2 oxygen-ion conduction in solid-state electrolytes (ZrO ₂) _x (Y ₂ O ₃) _{1-x} (≈ 100 μm)	99	volume ≈ 0.1 m ³ 50 rods each with 20 elements	1.5	—	power consumption 1 kW	porous, tubular or Zr-Ca-oxide. Pt-Zr electrodes thick) coated with U ₃ O ₈ support (10 μm thick 5 μm

4	4.1	90	1 kg salcomin can bind 35 l O ₂	1.5	—	no use, unfavorable thermal properties of salcomin and, with small instruments, much energy, needed for cooling	(cycle time e.g. 80 min) after a few hundred cycles, decreasing yield
Separation by reversible O ₂ adsorption to chemicals	in order to achieve adsorption Salcomin (salicylaldehyde cobalt ethylenediamine) is brought at a relatively low temperature and high gas pressure into contact with normal air and then, for desorption, subjected to low pressure and heated to e.g. 90 °C		volume 1 m ³ mass 180 kg			power consumption 2 kW	
5		40		1.5	—	no use, still slight selectivity S=5 to 10 required	(literature on "artificial blood")
Separation by varying gas solubility in liquids	special liquids dissolve more O ₂ under pressure than N ₂ . Below atmospheric pressure, the O ₂ is released again (perfluorinated hydrocarbons)						
6		90	production from 12 kg chlorella	1.5	—	no use, extravagant in maintenance, large dimensions	
Production by algae	algae, like chlorella pyrenoidosa, produce oxygen by photosynthesis						

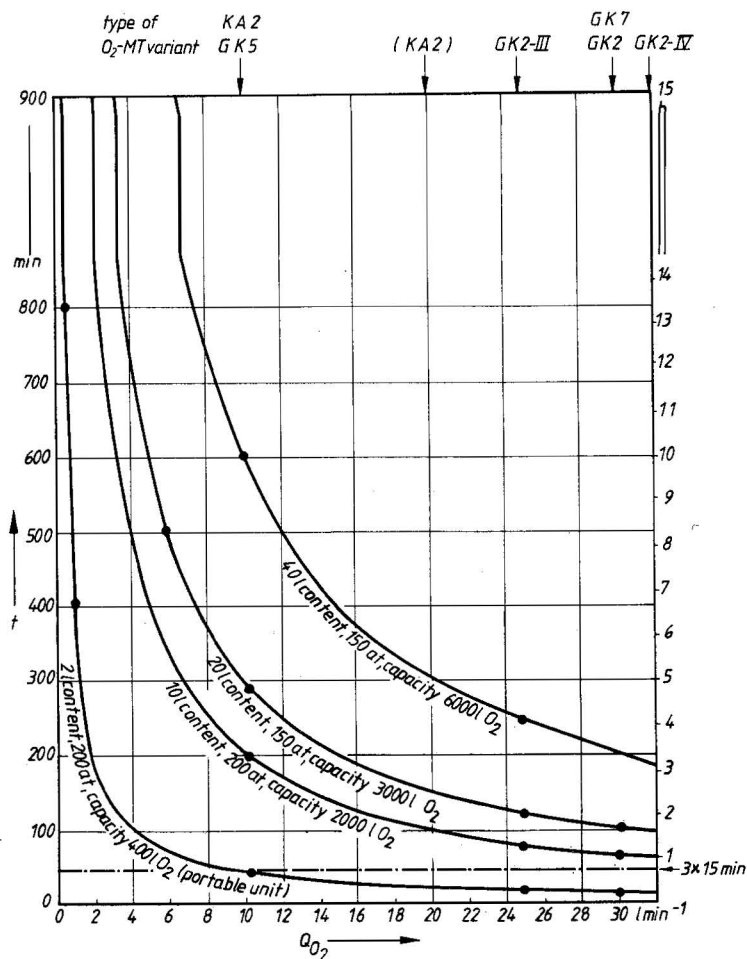


Fig. 177 O_2 delivery capacity of various standard-sized O_2 pressure cylinders expressed as the time t during which a certain O_2 flow $\dot{Q}_{O_2}$ can be maintained. On the upper abscissa the O_2 demand of further O_2 -MT variants is indicated (cf. Fig. 176)

riegelskreuth, FRG), and Draeger (Lübeck, FRG). Since the difficulties in obtaining workers to transport large steel cylinders are constantly increasing, the development of the devices described in the following two para-

graphs for deployment also in cure institutions and clinics should be warmly welcomed, provided that their performance is sufficient to deliver the O_2 flow for the intended O_2 -MT procedures.

3.2.4 Oxygen provision from zeolite separators

O_2 provision from zeolite devices is at present the most developed of the systems given in Tables 19 and 20. The " O_2 Selector", which was developed in 1973 in our Institute and has since then been tested medically, should be named here. This historical device, which is characterized by an alternating operation between two cylinders and a pressure swing between atmospheric pressure (adsorption) and reduced pressure (desorption), is shown in Fig. 179.

The data given in Table 19 show that this apparatus is just in the position to supply the O_2 flow named in Paragraph 3.1 (recently established to somewhat higher), for both the 36 h

and the 15 min O_2 -MT procedure. It is of great practical significance that this device, with its O_2 output adapted to all variants of the O_2 -MT, will be put on the market in 1988 by Hauni-Werke (Hamburg, FRG) in a large series of 10 000 and at a reduced price thanks to support from the Kurt Körber Foundation (cf. Fig. 180).

The O_2 generation of the less efficient devices usual today is *not* sufficient. This should not surprise us, as the smaller devices were created for a different purpose, namely for long-term therapy in the home, where a smaller O_2 flow is adequate. The firms DeVilbiss (USA), Draeger (Lübeck, FRG), Weinmann (Hamburg, FRG)

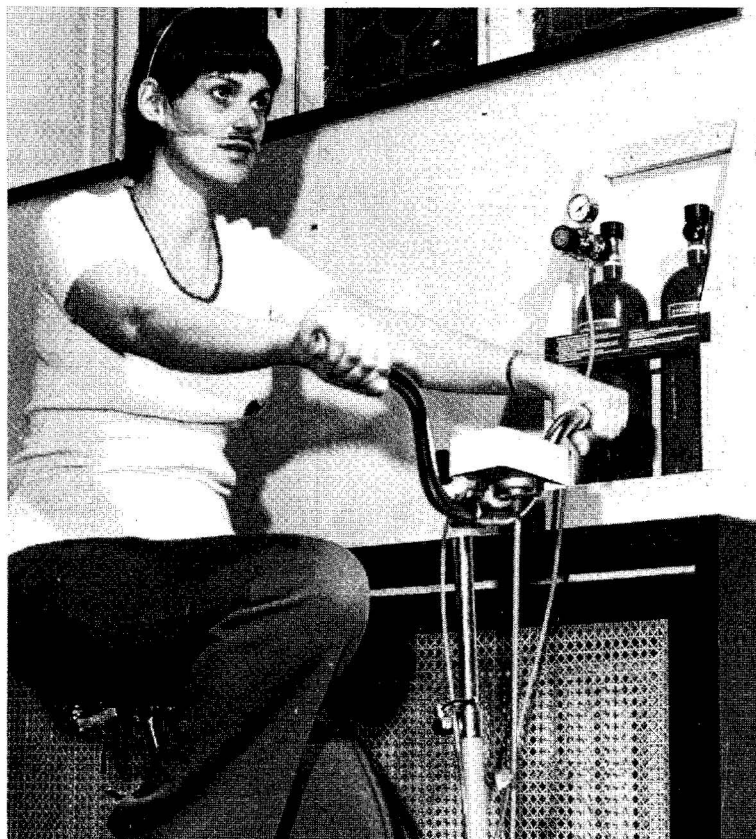


Fig. 178 2x2 l light steel pressure cylinder unit providing 800 l O_2 (Oxyparat Allihn, Munich, FRG) in the application of O_2 MT with bicycle ergometer

etc. also brought out small devices around 1982, and Buderus (FRG) in 1985.

The following lines should give some details for the orientation of the reader on the *technical solution of the Dresden "O₂ Selector"*, especially designed for the requirements of the O_2 MT. The device supplies in 22 h in its product gas the same amount of additional oxygen as is contained in a 40 l (150 at) pressure cylinder. For gas separation this device applies the principle of selective and reversible nitrogen adsorption on special zeolites (molecular sieves). It uses the zeolite type KX and, recently a fine-pore type from the Elektrochemisches Kombinat (Bitterfeld, GDR). The atmospheric nitrogen is adsorbed and desorbed by changing the pressure. In the adsorption phase O_2 -enriched air remains as the product gas of the device [286, 295]. The "O₂ Selector" contains two vessels filled with zeolite, which are cyclically and sequentially evacuated, flooded and rinsed.

The speed with which the steel cylinder will be partially replaced by zeolite devices or anal-

ogous systems in the envisaged medical and therapeutic facilities, will depend on the price, i.e. therefore also very much on the scale of their production. As far as their technology is concerned, they do not need to cost much more than household devices of similar size, washing machines for example.

The precondition for a transitions of the O_2 MT into broad use in medicine and the health service is a low price for devices which can provide oxygen at a flow of 5 l/min and which can be equipped with economical storage accessories for, e.g. $30 \times 15 = 450$ l O_2 (filling time 1.5 h; sufficient for the 15 min O_2 MT quick procedure). A low price will make possible the utilization of this universal therapy for poorer sections of the population, for procedural repetitions in the home, for places without O_2 provision from pressure cylinders, and for doctors and patients in developing countries. Thus the decision of Dr Kurt Körber, already mentioned, to produce 10 000 devices of this type in the Hauni-Werke (Hamburg, FRG) subsidized from the means of the Körber



Fig. 179 The first GDR zeolite operating O_2 selector device, developed in the Manfred von Ardenne Research Institute, Dresden, GDR, 1973. Maximal O_2 provision 5 l/min at an enrichment factor of 60 vol.%. This prototype has been further developed according to Table 19 in order to meet the grown O_2 demand of the different O_2 MT variants. As mentioned in the text, the new version having a 450 l storage unit is manufactured at a large scale in the Hauni-Werke, D-2050 Hamburg-Bergedorf, FRG

Foundation, has opened the door to new ways of helping people against many diseases, problems and complaints, and to ways which often prevent illness by the prompt elimination of their cause (energy deficiency).

It is possible that the conditions for the development of economical and smaller devices for O_2 provision will improve even further in the next ten years. It has already been possible to perfect the separating properties of the zeolite

molecular sieves by doping (e.g. with ZnO , SnO_2 etc.) and also O_2 -selective membranes, discussed in the next paragraph, by coatings of the most varied kinds (Fraunhofer Institut, Stuttgart, FRG; Toshiba, Japan; Matsushita Electric Industry, Japan). Zeolite separators, fed with O_2 -enriched air coming from preset O_2 -selective membranes of high performance, are also already under discussion in order to improve yield and flow rate.

3.2.5 Oxygen provision from membrane filter devices

The process of O_2 separation by means of selective permeation through thin membranes seems in principle to be simple, and requires little energy. Research encountered difficult

technological problems, however, since the necessary permeation rates can only be achieved using a relative large area of exceptionally thin membranes. For this reason a commercial

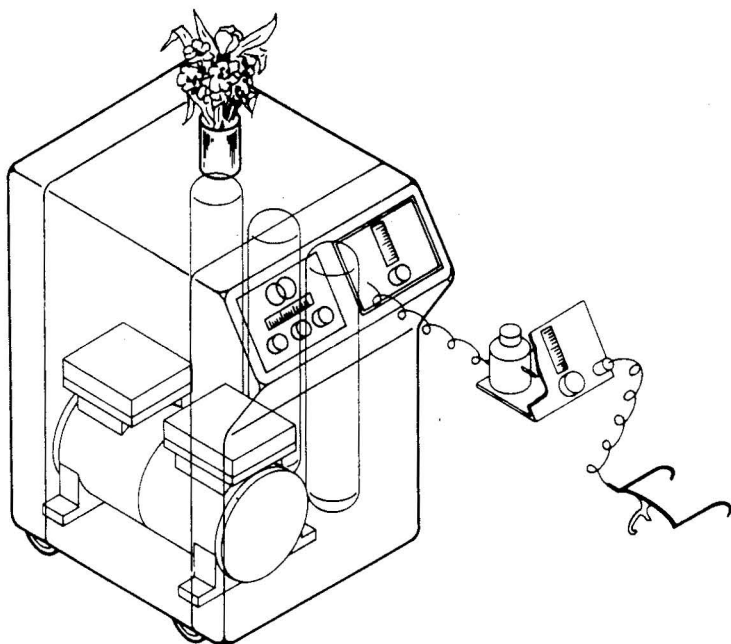


Fig. 180 Diagram of the O_2 selector basic device with O_2 provision adapted to the O_2 requirements of most O_2MT variants. Development: HAUNI-Werke, Hamburg-Bergedorf (FRG) in co-operation with the M. v. Ardenne Research Institute Dresden, GDR (5 l/min oxygen; weight ca. 40 kg; height x breadth x depth: 70 cm x 45 cm x 50 cm); large-scale production 1988

device [290], the data of which were given in Table 20, column 2.1, is as yet only in its preliminary stages. Nevertheless the state of the developments leads us to assume that the process has a promising future.

The principle of the membrane filter process is shown in Fig. 181. The initial gas mixture, normal air, passes over the membrane and leaves room 1 as O_2 -depleted air, whilst in room 2, on the other side of the membrane, O_2 -enriched air can be withdrawn. In order for this to function, a pressure gradient ($p_1 > p_2$) must exist above the membrane. In order to achieve this, either the feeding air is compressed, or the product gas is sucked off. The permeation through the membrane is deter-

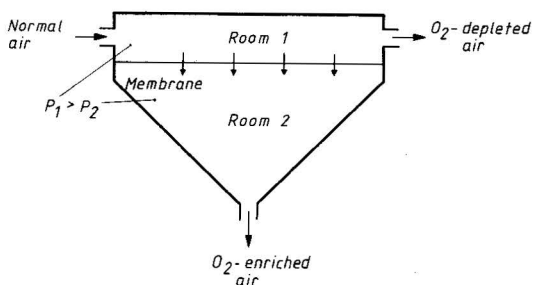


Fig. 181 Principle of O_2 enrichment with selectively permeable membranes

mined by the properties of the material and is different for each gas component. For the component i , the permeation coefficient amounts to

$$Pr_i = \frac{\varphi_i \cdot x}{A \cdot \Delta p}$$

in which

φ_i represents the flow of the component i through the membrane (permeating volume per time unit, corrected to standard conditions in terms of p and T),
 x the membrane thickness,
 A the membrane area, and
 Δp the pressure difference above the membrane.

A series of materials, e.g. silicon rubber and organic polycarbonates, are of particular interest for O_2 separation by means of a membrane.

Silicon rubber has a large permeation coefficient of $Pr_{O_2} = 1.28 \cdot 10^{-11} \text{ cm}^2/\text{Pa} \cdot \text{s}$, but the separation factor is small: $Pr_{O_2}/Pr_{N_2} = 2.2$.

Polycarbonates, however, have a permeation coefficient of $Pr_{O_2} = 3.75 \cdot 10^{-13} \text{ cm}^2/\text{Pa} \cdot \text{s}$, but makes up for that by a separation factor of $Pr_{O_2}/Pr_{N_2} = 4.8$.

For a given flow φ_i , with a given thickness x and a given pressure difference Δp , the size of the permeation coefficient Pr determines the membrane area A required; the larger Pr is, the

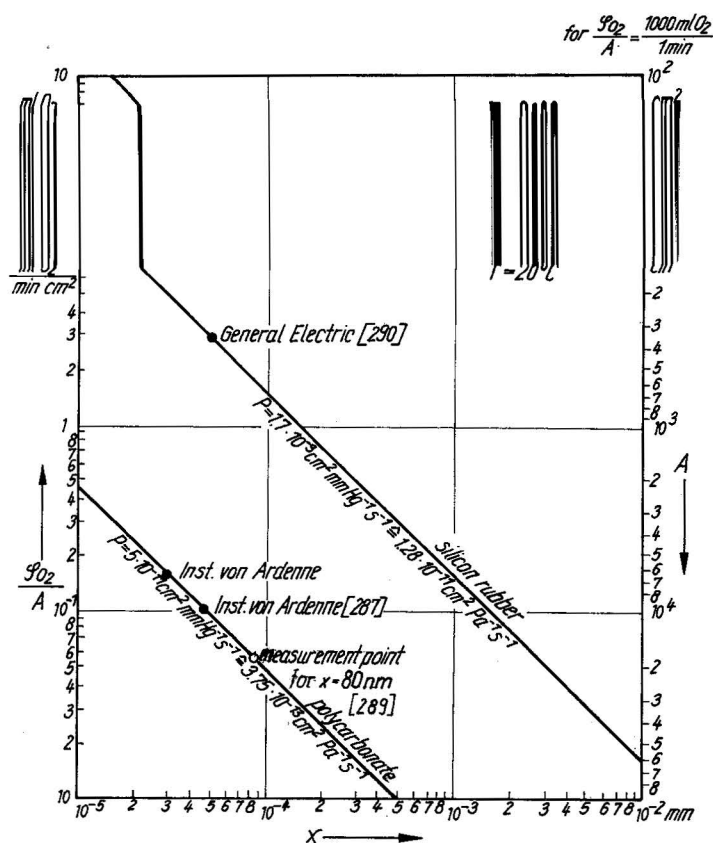


Fig. 182 O_2 volume per cm^2 (A) permeating a membrane at 150 mmHg = 20 kPa pressure difference, as a function of the membrane thickness x for polycarbonate and silicone rubber membranes. P = permeation coefficient

smaller this area can be. The required area A can also be reduced by reducing the membrane thickness x (important factors here are: high tear resistance of the material and the necessity of support structures). Figure 182 illustrates the facts concerning membranes of silicon rubber and organic polycarbonates.

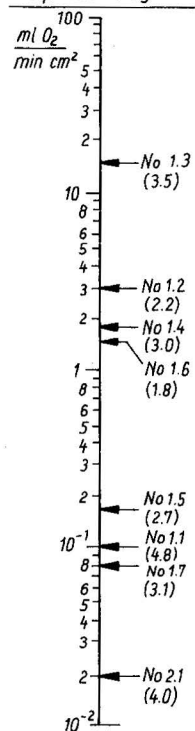
The separation factor Pro_2/PrN_2 determines the maximum attainable concentration of oxygen in the product gas [290]. *Silicon rubber membranes and polycarbonate membranes technically make possible an oxygen enrichment of approximately 30–35 and 39–51%, respectively.*

The prototype of a commercial device of this kind, already mentioned in Table 20, column 2.1, applies silicon rubber membranes. The use of a membrane having a thickness of only 50 nm is made possible by a microporous support. A membrane area of $A = 400 \text{ cm}^2$ is required for an O_2 provision of 1.5 l/min. The product gas side (room 2) is evacuated for this to 1/5 at (20 kPa). However, the resulting gas mixture (10 l/min) contains only 33 vol% O_2 . Using somewhat more stable polycarbonate membranes (Table 20, column 2.2), the same level of O_2 provision under comparable pressure conditions requires a membrane area of $A = 1 \cdot 10^4 \text{ cm}^2$. The oxygen concentration is here 46 vol%.

The production and mounting of the membranes for experimental purposes was very difficult as, with the exceptionally thin layers, there should be no defects or leaks. In order to produce the membrane, a diluted polymer solution was layered on the surface of highly purified water, as in electron microscopic preparation technology. The solvent evaporates and a thin polymer film remains on the water surface. Then this membrane was laid on a mount by carefully lifting a grid previously submerged (as with a strainer) [296]. The pore size of this mount was some tens of μm . Large membrane areas could only be achieved using this process by joining of such small membrane units, whereby the relation of the membrane area attainable to the construction volume of the entire assembly was very unfavorable.

Nowadays very homogeneous, pore-free, ultra-thin polycarbonate foils are produced on a large scale (Bayer, Leverkusen, FRG), cf. also [287]. The great mechanical stability of such membranes (tear resistance 78.5–90 N/mm²), in comparison with silicon rubber 7 N/mm²) allows the application of considerably higher working pressures. Future developments in this field will therefore tend to create devices working with polycarbonate or, probably, with doped foils of even more increased separation efficiency.

O_2 permeation rate at
 $\Delta p = 150 \text{ mm Hg}$:

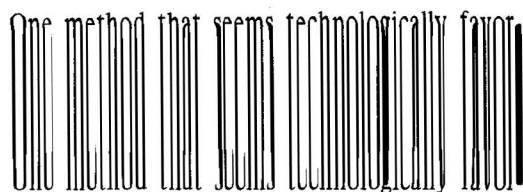


System	No.	support for membrane or porous material	thick- ness X	separating membrane	thick- ness X	pore diameter (μm)		coating		O_2 -permeation rate at $\Delta p = 150 \text{ mm Hg}^1$	separation factor	References (Remarks)
		material	μm	material	μm	before	after	substance	thick- ness μm	ml O_2 / min cm^2		
1 without pores	1	poly- carbonate		poly- carbonate	0.05	—	—	—	—	0.1	4.8	Fig. 182 Inst. von Ardenne 1977
	2	silicon rubber		silicon- rubber	0.05	—	—	—	—	3.0	2.2	Fig. 182 [290] (Development General Electric, New York, USA 1976)
	3	polypropylene (porous) with 2 layers of butadiene rubber		polyoxyphenylene film precipitated from benzene	<0.05	—	—	—	—	14.0	3.5	(Separating membrane between the butadiene rubber layers)
	4	polypropylene (porous) with butadiene rubber		dimethylsiloxane/ hydroxystyrene copolymer/vinyl pivalat-copoly- mer	<0.05	—	—	—	—	1.8	3.0	Matsushita Electric Ind. Co., Japan 1982 (patents)
	5	polysulfone (porous) impreg- nated with siloxane dissolved in $C_2H_2F_2$ and heated	60		<0.05					0.15	2.7	siloxane layer 0.7 μm (5% sol. of copolymer in $C_2H_2F_2$) on water
	6									1.68	1.8	O-A Machinery Cora. Japan "Oxygen Enricher" 1986 7.2 kg 28% O_2 2.6 l/min
	7	hollow fibre bundles spun from ethylcellu- lose solutions and coagulated	52			—	—	—	—	0.08	3.1	(asymmetric hollow fibres (patents))
	8											
2 with pores	1	poly- carbonate	5	—	—	0.1	0.03	sputtering of SnO_2 and other metal oxides	0.2	0.02	4.0	Toshiba Corp., Japan 1982 (patents)
	2											
	3											

Fig. 183 O_2 permeation rate at $\Delta P = 150 \text{ mm Hg}$ (20 kPa) and separation factor Pr_{O_2}/Pr_{N_2} in some recent membrane systems for O_2 enrichment

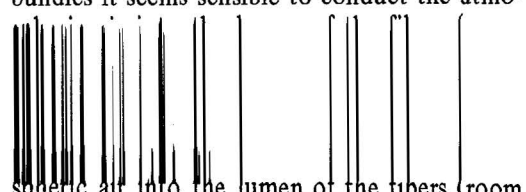
¹ Corresponds to the normobaric O_2 partial pressure

Figure 183 shows a compilation of the data of recent membrane systems for O₂ enrichment.



able for the production of stable membrane systems with large effective surfaces in a compact design is the *hollow fiber bundle*, as usual in dialysis machines for extraction and purification of fluids. An effective membrane area of 1000 m² could be obtained using, for example, a bundle of hollow fibers with a wall thickness of 4.5 μm (!) and an external fiber diameter of 18 μm, with a bundle dimension of 30 cm length and 30 cm in diameter. With a pressure difference of 700 mmHg (98 kPa), 8 l/min product gas with an O₂ concentration of 40% could be gained. Hollow fiber bundles made of polyester, with an external diameter of 36 μm

and a wall thickness of 9 μm [297] are commercially available. When utilizing hollow fiber bundles it seems sensible to conduct the atmo-



spheric air into the lumen of the fibers (room 1). The product gas is then taken from the interstice (room 2), which surrounds the fibers in the bundle [289].

The sandwich principle should be probably even more effective in terms of constructing compact arrays with large effective separation surfaces.

The distant area of development is a *small, selective respiratory gas filter for oxygen*, which can manage without the technical production of pressure differences, and which is so designed that the patient can easily carry it around with him.

3.3 Technology and results of the HOT* methodology, or the oxygen activation methodology

3.3.1 HOT* methodology

It has been repeatedly pointed out that the method of *hematogenous oxidation therapy* (HOT) according to Wehrli [222] can contribute to the permanent improvement of the blood microcirculation, especially when combined with procedures of the O₂MT. This combination succeeds easily and considerably reduces the risk to the patient when devices are used, which, thanks to improvements in the UV irradiation system, *do not require blood foaming* [223]. The term *HOT** (with an asterisk) was introduced for this improved variant. Previous decades saw hypotheses of the most varied kinds as to the physiological effector mechanism of this method (which is very successful in the treatment of peripheral circulatory disorders in the lower extremities), for the correctness of which there was, however, no convincing evidence. This disadvantage led to widespread scepticism. This reservation was made groundless by our discovery in 1980 [50] that the HOT* procedure leads to a significant drop in the PO_{2-ven} , at rest, for some days and that, when the procedure is performed three times, for example, the utilization coefficient η of the O₂ binding capacity of the blood, and thereby also the O₂ offer to the body tissue, can be roughly doubled for a time, compared with the initial condition.

This provided *evidence*, backed up by measurements, of a *strong effect attributable to HOT**. The mechanism that primarily sparks off this effect is still unknown. Today we suppose it to

be the catalytic influence of short-lived oxygen radicals, which arise during the irradiation of the blood with short-wave UV light and then contribute to the detumescence of the endothelial cells in the capillaries, with the result that the narrowings in cross-sections disappear. We tend to this view because signs very similar to those using HOT* were observed in the influence of ozone on human blood [224, 225]. The same must be assumed for the application of activated oxygen (non-invasive method) and according to reported findings (e.g. Jacobitz), also for Regelsberger's so-called "oxygenation therapy" [226, 227]. It is striking that both *the application of HOT* and ozone can greatly alleviate or even eliminate peripheral angio-organopathies*, in particular, of the most various stages. This indicates a difference in the effect on the one hand, and the O₂MT procedures which influence the whole organism on the other, which could be explained in the short-lived nature of the oxygen radicals.

The simple device for the implementation of the HOT* procedure is shown in Fig. 184. The quartz cuvette for blood irradiation is mounted on the top of a chassis which is covered with a lucite lid. The cuvette encompasses a volume of 75 · 22 · 1 mm³ and has a taper at both ends for attaching silicone tubing. The injection needle (for withdrawal and reinfusion of the patient's own blood) is fixed at one end of the tubing, a 50 or 100 ml syringe at the other. The *special UV lamp HNU6*, including the ballast resistor

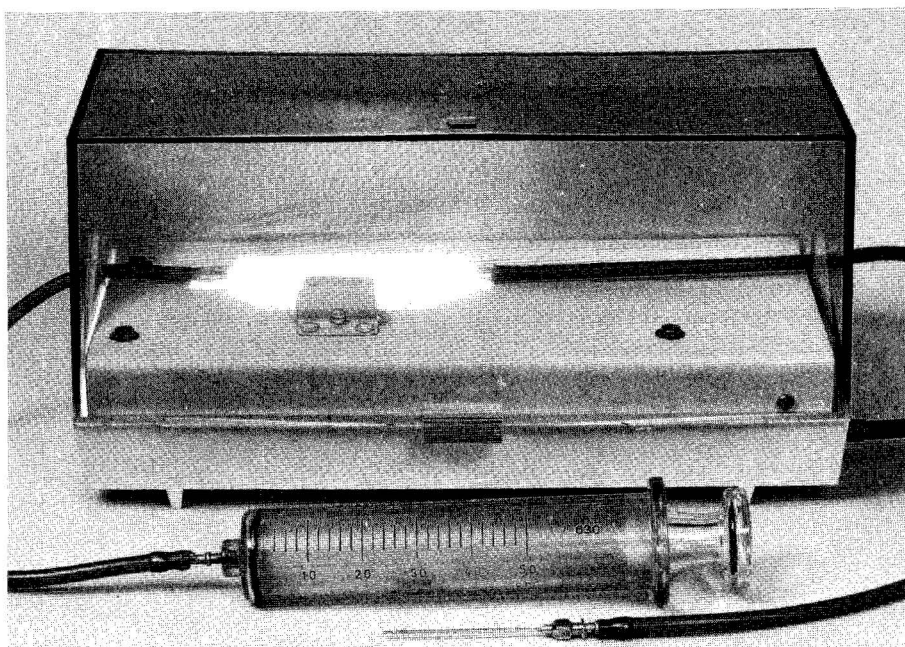


Fig. 184 Instrument for the implementation of the hematogeneous oxidation therapy (HOT*) without blood foaming. HOT device Thelta-Ultramed B 1, with quartz burner (for generation of short-wave UV radiation) and thin layer quartz cuvette for the irradiation of the patient's own blood. Manufacturer: VEB Thelta Elektroapparate, DDR-6060 Zella-Mehlis. General representative: EMC Erzeugnisse für Medizin und Chirurgie, Goebbelgasse 100, D-5100 Aachen, FRG

VUV6, is mounted in the chassis below the cuvette (not visible). The maximum emission of the low-pressure discharge is at 254 nm.

After the device has switched on, blood (1 ml/kg body weight) is slowly and carefully drawn from the cubital vein by pulling the plunger of the syringe. The blood flows through the cuvette into the syringe, is mixed there with prefilled 3% sodium citrate solution at a ratio of 10:1 (or 15:1 in case of difficult venipuncture) and is reinjected in the same way. Hence, the blood passes the irradiation cuvette twice; the whole procedure is finished within 5 min.

The quartz cuvette, including the silicone tubing, should be vigorously rinsed immediately after each HOT* treatment in a disinfecting solution, perhaps 30% H_2O_2 , and distilled water in succession. Should there still be any deposits, they can be removed with 20% NaOH or KOH (caution!) or, better, with Deconox 11 Universal (Borer, Solothurn, Switzerland). Then the cuvette and the tubing are thoroughly rinsed with distilled water and sterilized up to 200 °C by hot air or steam. The cuvette should

be handled without touching its windows in order to avoid fingerprints, which reduce the UV permeability.

Figure 185 shows the implementation of the HOT* procedure with simultaneous O_2MT measures. Several results of the kind shown in Fig. 186 challenge us to test whether the combination with HOT*, or with application of activated oxygen, could be used to *speed up and intensify immediate aid in emergencies in non-able-bodied patients*. The combination procedures should be very advantageous in chain smokers, as we usually found very low PO_{2-art} levels in these patients with O_2MT alone, which often rose significantly after HOT* or application of activated oxygen.

Figure 187 shows a summary of results before and after 1 to 3 reinfusions of the patient's own UV-irradiated blood (HOT* procedure). Unfortunately, the duration of the effect of the invasive HOT* on the PO_{2-art} is, according to our measurements, limited to a few days. Nevertheless, HOT* can be assessed as a valuable supplement to the O_2MT in selected indications (e.g. combat of peripheral circulatory disorders)

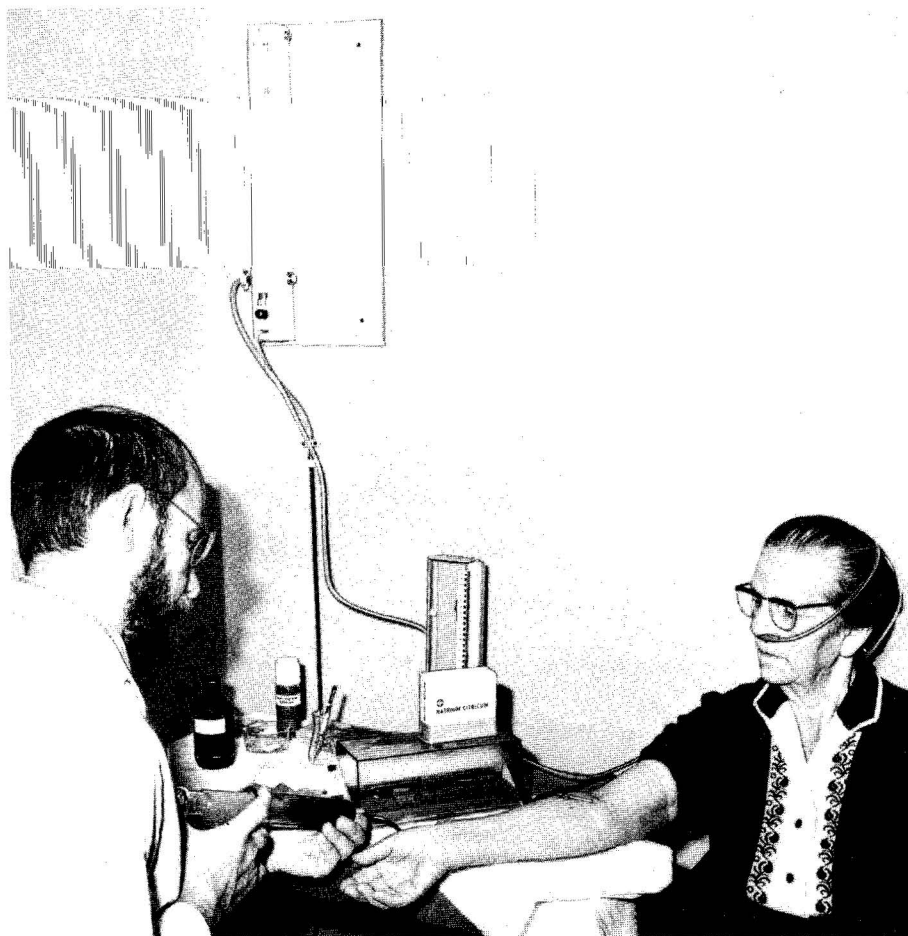


Fig. 185 Implementation of the combination procedure HOT* plus simultaneous O_2 multistep measures

[228]. Because of the greater relative steepness of the O_2 dissociation curve in the region of the venous PO_2 (factor of 10), the discovered drop in the PO_{2-ven} in particular contributes to a great improvement in the utilization factor η of the O_2 binding capacity.

Figure 188 shows examples of the raising of the

PO_{2-art} by three treatments with HOT*. Although the effect lasts only a short time, in this case only during the days of treatment, it can be used particularly in partially O_2 MT-resistant patients (PO_{2-art} non-responders) in order to raise the PO_{2-art} under O_2 inhalation for the first sessions of the 36 h O_2 MT procedure.

3.3.2 Oxygen activation methodology. Oxygen ionization

The O_2 activation methodology has as yet been little researched [298]. With it, O_2 flows to the applicator after passing an ionizer tube as in Fig. 189, were a silent medium voltage discharge partially activates the oxygen. In order to keep losses due to the recombination of radicals low, the activator or ionizer is situated as near as possible to the applicator. EMC (Aachen, FRG) offers a physically optimal version, in which the ionizer is built into the mask applicator. The activated O_2 goes direct to the lungs by inhalation. That is where the highest

concentration of activated oxygen species, and thus also their strongest catalytic influence on the vessel wall cells of the capillaries, exist. It is therefore not surprising that it is *mainly the increase in the resting PO_{2-art} that is improved* using this simple, non-invasive method, which was particularly promoted by Engler. Impressive therapeutic effects have sometimes been attained in patients with a damaged arterialization function of the lungs.

An example of this is given in Fig. 190. A somewhat smaller increase in the PO_{2-art} , at rest,

Cause of crisis		Trauma
O_2 -multistep measures	drugs i.v.	$\text{vit B}_1, \text{vit C, Mg orotate (oral)}$ O_2 -flow $5-10 \text{ l/min}^{-1}$ mask applicator HOT* Continuation until end of acute crisis.
	O_2 -inhalation	
	HOT* $\times 1^1$	

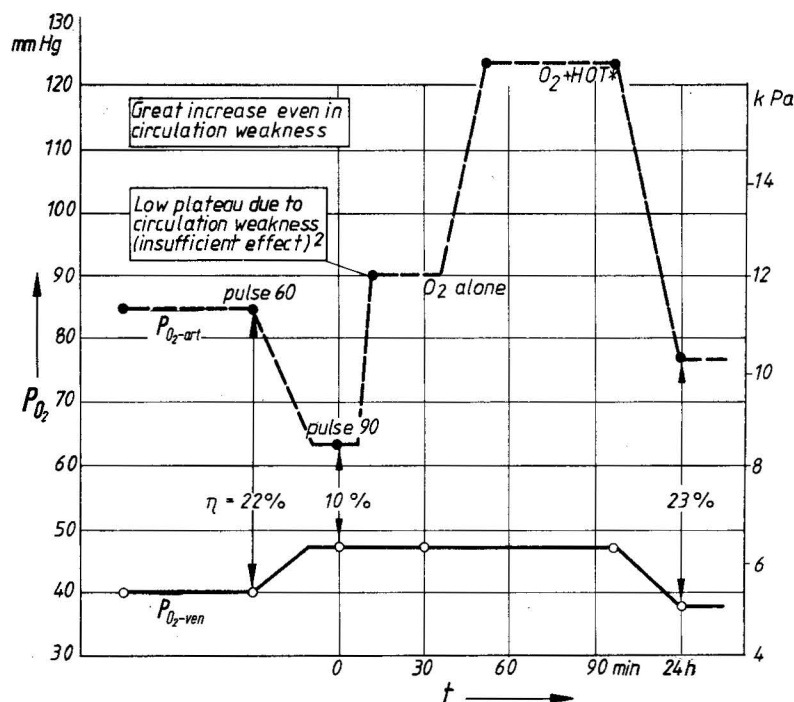


Fig. 186 Combination procedure with simultaneous O_2 multistep measures and HOT* procedure for immediate aid in non-able-bodied patients

¹ If vena cubitalis is collapsed, the vena femoralis or the (non-collapsing) vena anonyma is to be used for the procedure

² Particularly pronounced in chain smokers

resulted from a series of treatments with volunteers, as in Table 21.

Figure 191 shows data on the toxic effect of ozone, as well as measurements of the ozone concentration in the respiratory gas after passage through a corona O_2 activator.

Due to the not insignificant extra expense involved (cost of the device) the method of ionization of oxygen is only applied relatively rarely, although it can help in special cases (e.g. in chain smokers) by the additional raising of the P_{O_2-art} at rest, during treatment.

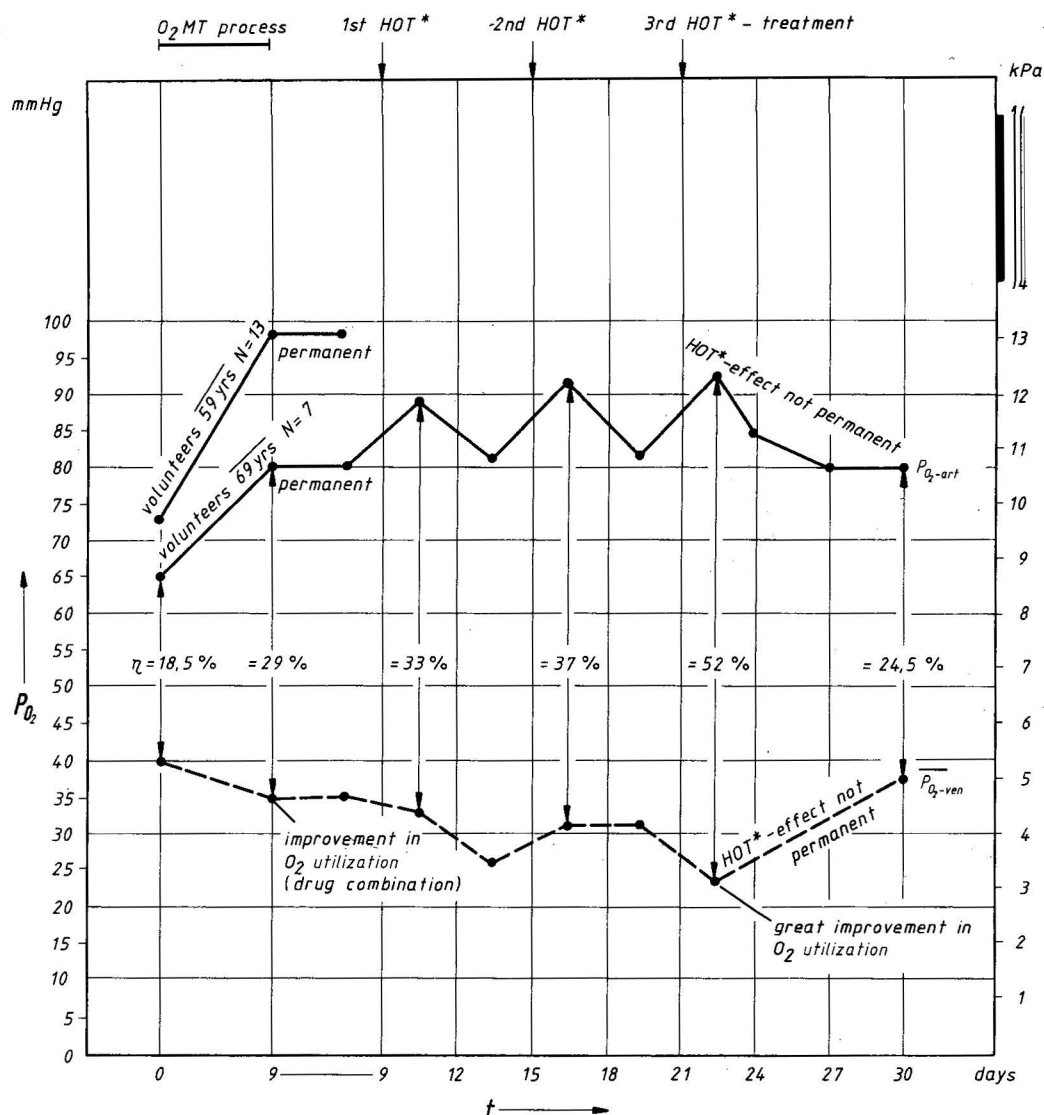


Fig. 187 Measurements of the increase in the arterial P_{O_2} and decrease in venous P_{O_2} by means of the O₂ multi-step regeneration procedure in combination with threshold HOT* treatment. η = utilization of the O₂ binding capacity of the blood

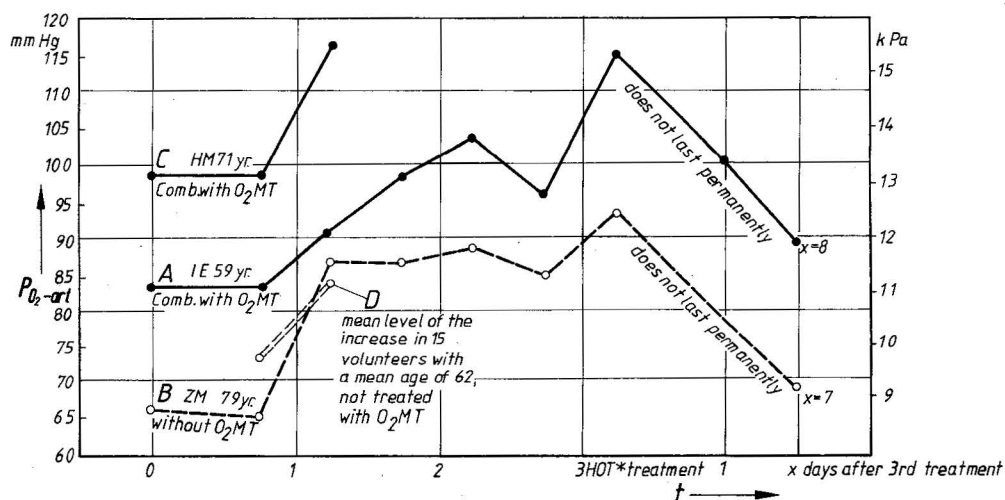


Fig. 188 Measurement examples of the rise in the arterial P_{O_2} with threefold treatment by reinfusion of the patients' own UV-irradiated blood, HOT* (A, B). No permanent effect, but the effect lasts long enough to intensify the O₂ multistep regeneration procedure. Increase in P_{O_2-art} under O₂ inhalation by means of HOT* during the first three sessions of the procedure

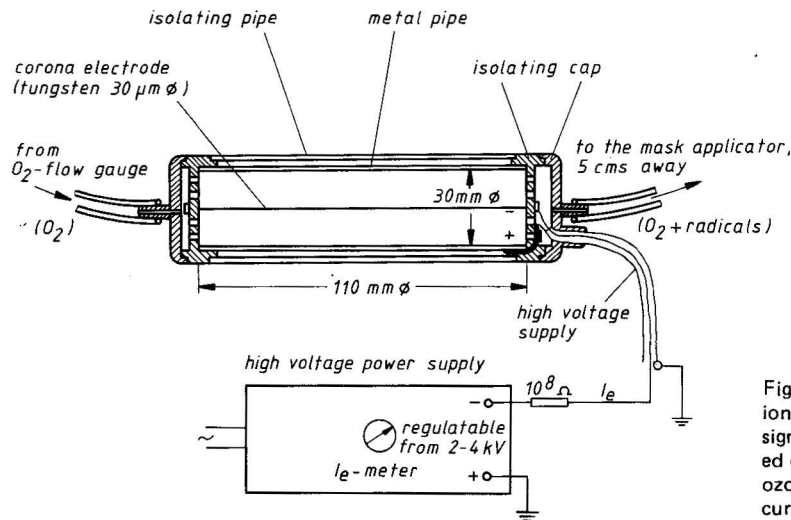


Fig. 189 Section through the O_2 ionization tube (experimental design) for the production of activated or excited oxygen in a corona ozonizer. Intensity of discharge current $I_e \approx 1$ to $8 \mu A$

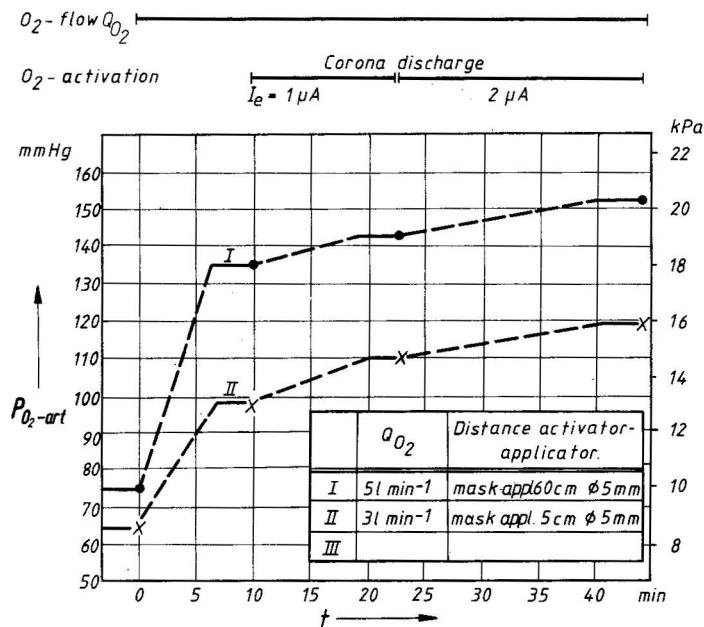


Fig. 190 Measurements of the increase in the arterial PO_2 appearing under O_2 inhalation, when the oxygen entering the applicator is previously activated in the O_2 ionization tube at a given I_e as indicated. Patients I and II with healthy lungs

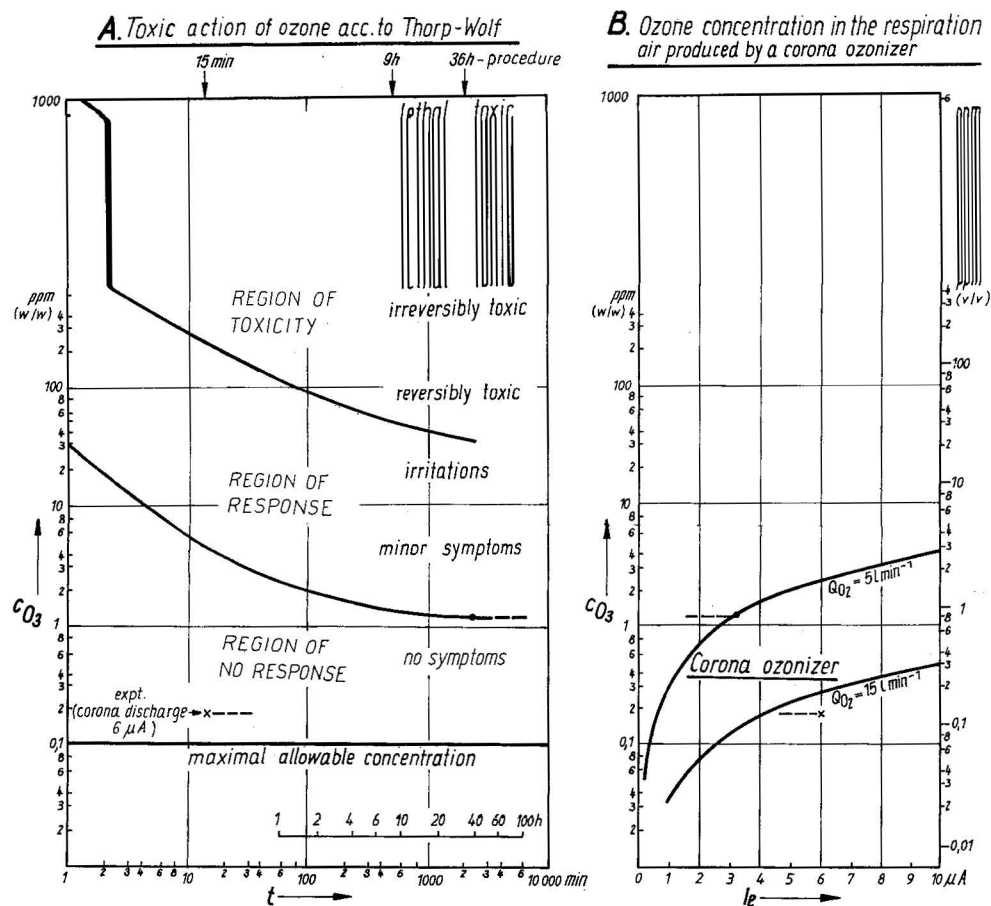


Fig. 191 The toxic effect of various ozone concentrations c_{O_3} as a function of the exposure time t (A), and the ozone concentration produced by means of a corona ozonizer, dependent on the corona discharge I_e in the applied oxygen (B). O_3 should mainly contribute to the "catalytic effect"¹

¹ No. of ion/no. of O_3 molecules $4 \cdot 10^{-12}$; ion concentration $2 \cdot 10^{-10}$ ppm

Table 21 The arterial P_{O_2} in 10 individuals, measured under resting conditions, before and after inhalation of oxygen at a flow rate of $\dot{Q}_2 = 4$ l/min using a mask applicator and after addition of ionised oxygen (7000 negative ions/cm³/s) from the BioKlion apparatus¹

No.	Sex	Age Years	arterial P_{O_2} , at rest			art. P_{O_2} difference caused by O_2 ionization mmHg	Remarks
			before mmHg	after addition of O_2 mmHg	after addition of ionised O_2 mmHg		
1	♂	64	58	88	98	+10	Vagotonic patient
2	♂	55	72	100	103	-3	
3	♂	47	78	140	148	-8	
4	♂	62	78	160	177	+17	Sympathicotonic patient
5	♀	54	72	168	174	+6	
6	♀	45	70	145	178	+33	
7	♂	54	64	90	90	±0	Chain-smoker, under β -blocker therapy
8	♂	61	74	94	102	+8	Condition after ultra-long distance competition (distress)
9	♂	52	76	108	117	+9	
10	♂	58	60	108	110	+2	
$\bar{x}$			55,2	70,2	120,1	+9,6	
$\pm S\bar{x}$				2,28	9,55	11,29	3,01

¹ Manufacturer: B. Wirtz, D-5168 Nidereggen-Abenden, FRG

3.4 Technology of the measurement of P_{O_2} in living tissues and in blood

3.4.1 Problems of P_{O_2} measurement in living tissues

The absolute value of the gain which occurs for tissue of the living organism during the O_2 MT and its individual steps was originally assessed from the increase in the concentration of the energy-rich phosphate in the brain, i.e. from the increase in the O_2 metabolism in animals [4, 242], cf. Fig. 133. This integral method is unsuitable for use in humans due to the necessary chemical processing of tissue samples. For humans we can use the method of direct P_{O_2} measurement in living tissue, which has been greatly improved in recent years [162, 166, 169, 272, 299–307], in order to perform quantitative studies. The problem of P_{O_2} measurement with microelectrodes in the intercapillary space of living tissue is presented in Fig. 192 and further commented on in Table 22. According to the chance location of the insertion of a microelectrode with a sensitive tip of only a few μm (e.g. closer to the arterial or venous

end of a nutritive capillary, or at a greater or lesser distance from the capillaries), different P_{O_2} levels, and also different ΔP_{O_2} levels will be measured.

Therefore the results of single *small-area measurements* only usually permit conclusions of a relative character. However, a large number of small-area measurements gives us a quantitative base for the frequency distribution of the P_{O_2} levels in the intercapillary space (Table 22, column 1.1.2), a result of great significance. Such measurements are complicated and time consuming, however, which makes them only acceptable for research. The *large-area measurement* of the tissue P_{O_2} , which can be carried out with less effort, should therefore be preferred when the aim is to gain guidelines as to P_{O_2} profiles in living tissue (diagnosis) and as to the effects of measures taken (therapy).

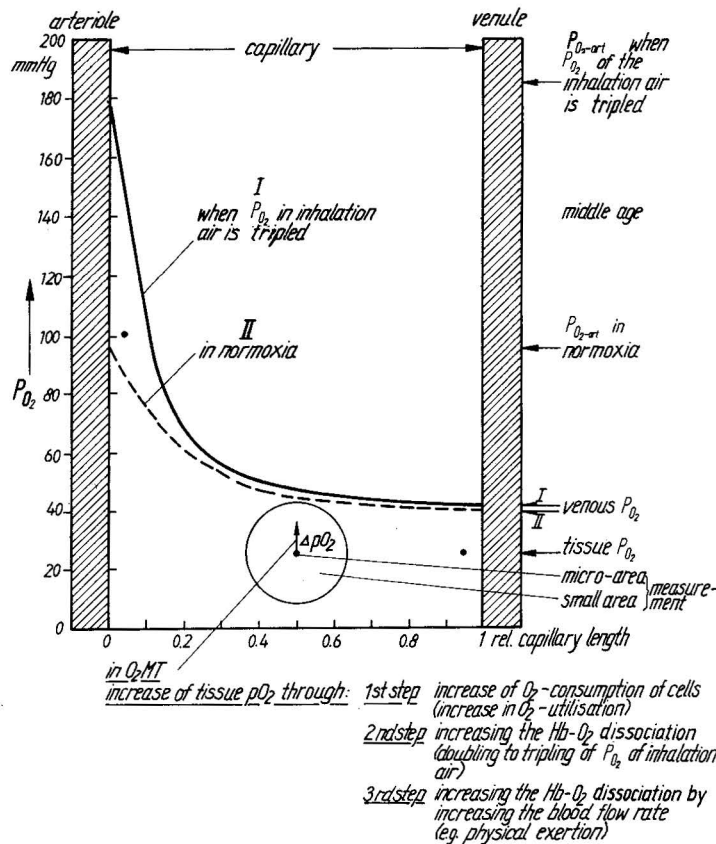


Fig. 192 Problems of micro-area or small-area P_{O_2} measurement in tissue between the arterial and venous ends of the supplying capillary (see also Fig. 97)

Table 22 Main types of PO_2 measurement in living tissue

Measurement principle	Type of PO_2 measurement		Area dimensions (approximate Φ)	Properties	Example	References (remarks)
1 PO_2 micro-electrodes (invasive)	1.1 micro-area measurement (sensitive tip 2–6 μm)	1.1.1 single measurement	intercapillary distance (only a few μm)	delivers absolute values (almost) slight injury low O_2 consumption		[32, 272, 299, 304] (absolute value according to position of puncture!)
		1.1.2 measurement of PO_2 distributions	intercapillary distance (only a few μm)	delivers absolute values (almost) as for 1.1	Fig. 98	[32, 166, 302] (very significant result)
	1.2 small area measurement (sensitive tip 6–20 μm)		intercapillary distance (10 to 30 μm)	especially for relative values	Figs. 157, 190	[159, 272, 308]
	1.3 large area measurement		intercapillary distance (50 to 1000 μm)	especially for relative values, but also for gaining absolute values for large areas	Fig. 128, 158	[159, 303, 308]
	1.4 <i>measurements in blood samples</i> "arterialized" capillary blood		sample volume ≈ 0.1 ml art: taken from ear lobe 10 min after rubbing with Finalgon forte ointment	especially for the reliable determination of the art. and ven. resting PO_2 . Delivers absolute values	arterial: Figs. 32, 37, 41 venous: Figs. 14, 61, 62, 126	[20, 21, 105, 157, 312] [6, 7, 50] (determination of η , the most important parameter of $O_2\text{MT}$)
	"non-congestive" venous blood		ven: taken from the unbound vena cubitalis	Fig. 195 and text	Fig. 200	
2 PO_2 macro-electrodes non-invasive transcutaneous measurement $PO_{2\text{-art}}$	2.1 large-area measurement of the arterial PO_2 with large-area PO_2 electrode heated to 43 °C		intercapillary distance (some mm)	delivers virtually the absolute values of the arterial PO_2	Figs. 201, 202, 203	[307, 308, 310, 311, 313, 317] (mostly thermal 43 °C arterialization)
3 PO_2 micro-electrodes non-invasive transcutaneous measurement $PO_{2\text{-art}}$	large-area measurement of the arterial PO_2 after "arterialization"		intercapillary distance (some mm)	delivers virtually the absolute values of the arterial PO_2	Fig. 200	development of the IvA (measurement at earlobe after 10 min arterialization by Finalgon ointment)
4 electro-chemical measurement	measurement with Clark type electrode in fluids in vitro or in vivo		see Fig. 100 when using the MO 10 instrument, one drop of blood	delivers absolute values well suited for studies of O_2 metabolism	Fig. 101 development: Hewlett-Packard 1970, USA	[2, 188] (especially for measurement and registration of PO_2 courses)
5 colorimetric measurement	spectral determination of the blood color		10 mm	well suited for measuring normal $PO_{2\text{-art}}$ and $PO_{2\text{-ven}}$ values		[316] (not suitable for measuring high $PO_{2\text{-art}}$ values!)

In very many cases it is more important or, at least, sufficient to measure the arterial and venous P_{O_2} levels, in order to detect or regulate their changes (example Fig. 62). Two methods can be used for this: the very accurate invasive method using "arterialized" capillary blood

[308] or venous blood [6], and the non-invasive method using P_{O_2} microelectrodes heated to approximately 44°C , which allow a *transcutaneous large-area measurement of the $P_{O_{2-art}}$* [162, 309–311].

3.4.2 Techniques of P_{O_2} measurements in living tissue

The principle of *polarimetric P_{O_2} measurement in vivo using needle microelectrodes* is shown in Fig. 193. For measurement, the electrode is a constituent of a polarometric electrical circuit. A direct current amplifier acts as an ammeter ($I = 10^{-5}$ – 10^{-12} A according to size of electrode). The plateau of the polarogram, characteristic for oxygen on gold surfaces (oxygen overvoltage), lies between -600 and -1000 mV. -950 mV is set as the normal level of the polarization voltage.

For calibration in vitro, the microelectrode (cathode) and the Ag/AgCl counter-electrode (anode) are immersed in a 0.2 molar NaCl solution which is equilibrated with a gas mixture of known P_{O_2} , e.g. air. After approximately 10 min the diffusion current remains constant, and its value is proportional to the concentration of the oxygen dissolved in the solution. This known value is set as the reference value on the display of the P_{O_2} meter.

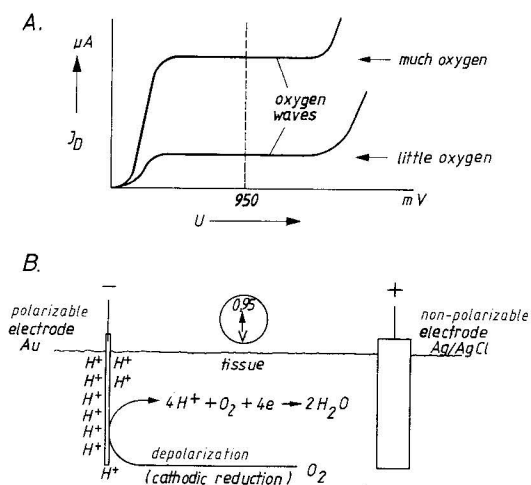


Fig. 193 Principle of polarimetric P_{O_2} measurement with oxygen electrodes. **A** Polarographic measurement by means of recording the diffusion current for oxygen waves with increasing voltage. **B** Polarometric measurement with constant voltage

Because the cathode itself consumes O_2 , an oxygen diffusion field is formed around it. This is dependent on the composition of the solution. This means that an electrode calibrated in vitro shows different values in vivo, even when the P_{O_2} is the same, so, strictly speaking, an absolute measurement using the open polarographic system is not possible as things stand at present. Needle electrodes can in general only be used for absolute measurement when the measurement and calibration medium correspond in terms of composition and geometric dimensions. This exists in measurements with a catheter if one ensures that the relations for calibration correspond to those for measurement. Great attention must be paid here to the pressure and flow conditions, as disturbance in the diffusion field immediately leads to different values. An absolute measurement in tissue is impossible; it is only possible to obtain the magnitude of the P_{O_2} and its dynamics.

In most application cases it is in fact not so much the absolute P_{O_2} , as the change in the P_{O_2} with the time, that is of more interest. We then refer, sensibly enough, to the starting level. The prerequisite for this is that the temperature of the site of measurement does not change during the measurement, and that the cathode remains in the same position. The necessary stability for a long examination can be easily achieved by securing the cathode, using adhesive plaster for example, and by the thermal isolation of the site of measurement, by wrapping it in gauze, for example.

According to investigations performed by others into the mean values and variations of the vascularization parameters (intercapillary distance, capillary length and diameter) [32, 166], the mean value of the *intercapillary distance* in kidney tissue with a good blood supply (renal cortex, rat) is $40\ \mu\text{m}$, and the maximum value is $50\ \mu\text{m}$. These values are somewhat higher in other tissue. In order to be able to determine the P_{O_2} levels within the intercapillary space, the dimensions of the sensitive tip (diameter and length) of P_{O_2} microelectrodes must be very small compared with

the intercapillary distance. Tip dimensions of between 3 and 6 μm are therefore required. Various construction forms meet this condition and allow small-area measurements, which are

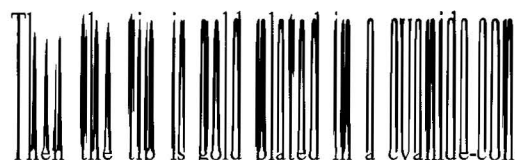


hardly disturbed by the O_2 pressure field [299, 300, 303, 306].

The task of producing very fine metal tips first arose in the construction of field emission electron beam generators [314]. Electrolytic etching has proven to be a reliable method [315]. The working regulations given there usually apply to tungsten wire. Tip diameters as small as 1 μm can be produced in an electrolyte, usually 1 M NaOH, by laying an alternating current (50 Hz) of 5–10 V between the tungsten wire and an auxiliary electrode of nickel or graphite. Any roughness of the surface can be smoothed out by annealing in a vacuum at approximately 2200 $^{\circ}\text{C}$.

According to the task to be undertaken, we use as a starting material molybdenum wires with a diameter of 0.1–0.5 mm. These are first cleaned by steeping in molten NaNO_2 and are electrolytically etched in an aqueous solution of NaNO_2 and $\text{K}_3[\text{Fe}(\text{CN})_6]$. Before the actual measurement tip (length between 1 mm and

40 μm) is etched, the wire is shrouded with molybdenum glass, produced by Fischer (Ilmenau, GDR) [320].



Then the tip is gold plated in a cyanide-containing solution, after the molybdates or oxides still remaining after the etching have been carefully removed by scouring. A hydrochloric acid-alcohol mixture and a 10% potash lye containing $\text{K}_3[\text{Fe}(\text{CN})_6]$ are used for this.

The in vitro calibration of the measurement system is undertaken in the way given above. All values are continuously recorded. Especial attention is paid to the exact fixing of the zero point and the determining of the residual current.

One PO_2 microelectrode for small-area measurements, produced in the way described, is shown in Fig. 194 A. Further PO_2 needle electrodes for small and large-area measurements are shown in Fig. 194 B and C [303, 159].

Fig. 195 shows a further type of PO_2 large-area electrodes in wire form, which allows subcutaneous and intracutaneous measurements [309] and which have proven their worth in research and clinical trials. This type of electrode is

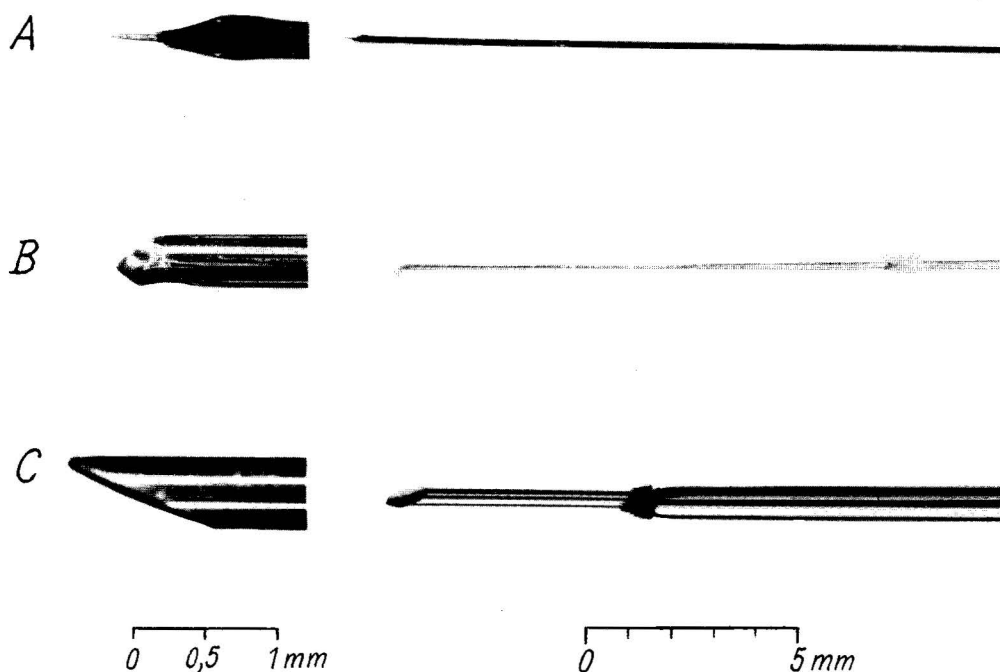


Fig. 194 Gold-plated PO_2 microelectrodes for micro-area measurements. (A: tungsten with tip radius $\approx 2 \mu\text{m}$), for small area measurements (B: molybdenum) and for large-area measurements (C: molybdenum) [304]. Specimens developed in our Institute

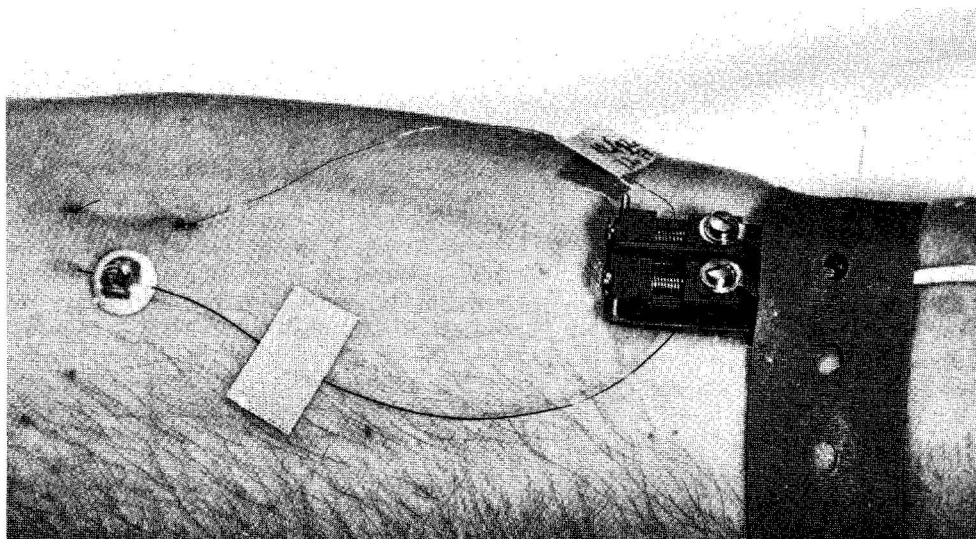


Fig. 195 Subcutaneous (above left) and intracutaneous (below left) variants of a large-area P_{O_2} electrode made up of gold-plated molybdenum wire, also anode plate and mounting on the volar side of the underarm [309]

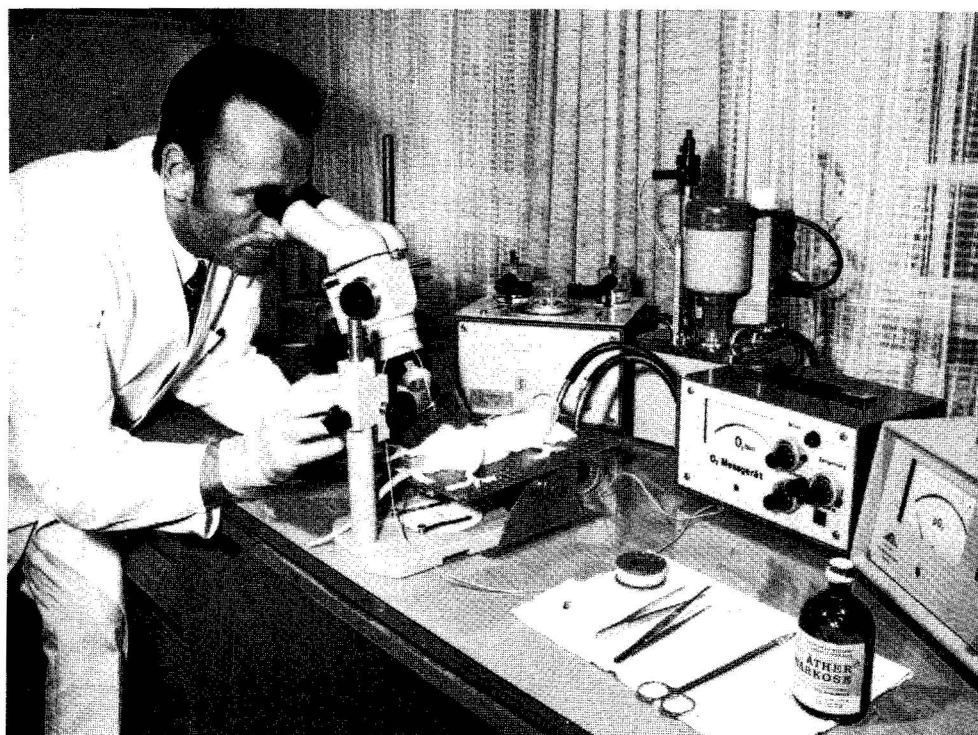


Fig. 196 Equipment for the measurement of tissue P_{O_2} levels as the basis of assessment of indications and effects of the oxygen multistep therapy

distinguished by its great mechanical and electrical stability in bedside application.

As far as good reproducibility of the values to

be obtained from these electrodes is concerned, the main thing is that the gold sheath is as *non-porous as possible* and that it *clings firmly to the support wire*. A great step forward has been made by the very recently developed vacuum depositing by high-rate sputtering using a ring crack discharge from a plasmatron source [318].

Figure 196 gives us a view of a *measuring arrangement for PO_2 values in small and large tissue areas*, for research using experimental animals.

Because of the *great diagnostic and therapeutic significance of the PO_{2-art} and PO_{2-ven} at rest*, already discussed, simple methods of precisely measuring these levels and their temporal course deserve particular attention. Their figures must be regarded as very important characteristic values of the momentary health status, roughly as important as the systolic and diastolic blood pressure. These levels should be determined much more often than in the past. Guiding values as to the daily profile of these characteristics are summarized in Fig. 33. It can be seen from the finding shown in Fig. 197 that it is very important that the patient does not speak during the measurement, no kind of stimulant (coffee, cigarettes etc.) can be taken, must strictly be observed. The patient should always be measured at the same time of day (cf. Fig. 10, e.g. at 3:00 pm, see Paragraph 1.1.5.2).

We have found that the PO_{2-art} is also *influenced by the body position*; the mean levels of the relative PO_{2-art} in 6 normal persons aged between 26 and 62 years were: sitting 1.00, standing 1.03; lying 0.98; lying with head and chest in low position 1.06. We recommend *measuring in a sitting position* as standard. The implemen-

tation of a procedure with head (and chest) in the low position can be useful in special cases (e.g. chronic severe bronchitis, first treat-



The invasive method with *blood taken from the earlobe*, which is virtually painless, is usually preferred for accurate measurements of the PO_{2-art} at rest. The *chemical hyperemization* (arterialization of the capillary blood) is normally undertaken by putting an ointment containing 25 mg nicotinic acid β -butoxyethyl-ester and 4 mg nonylic acid vanillylamide per gram on the earlobe of the patient. After 10 min complete rest (no conversation) the excess ointment is swept away, and a small incision is made using a disposable lancet, as is clinically standard. The blood is collected without air-bubbles in one or two heparinized capillaries for measuring the PO_{2-art} in duplicate [86, 219]. Measurements of the temporal course of this chemical "arterialization" are summarized in Fig. 198. According to [319], the same numerical values are obtained with capillary blood 10 min after application of the ointment as for the difficult and painful direct arterial puncture. For repeated registrations at intervals > 15 min, the ointment must be re-applied. When blood is frequently drawn from the earlobe over several years, the resulting cicatrization hampers the chemical "arterialization", resulting in too low PO_{2-art} levels being measured. The same is true if due to circulatory insufficiency or circular centralization the blood supply to the earlobe is poor. This error can be avoided, especially in the former case, if the earlobe is warmed to about $45^\circ C$ for approximately 2 min with hot water, and is moistened (by covering both sides of earlobe with a cloth soaked in hot water), immediately before applying the ointment.

We have already pointed out in Paragraph

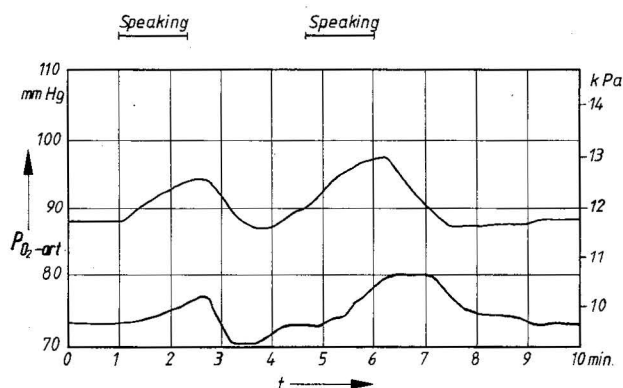


Fig. 197 Examples to show the increase in arterial PO_2 through speaking. Rule: silence during measurement phase. Increase by 4–9 mmHg = 0.53 to 1.1 kPa

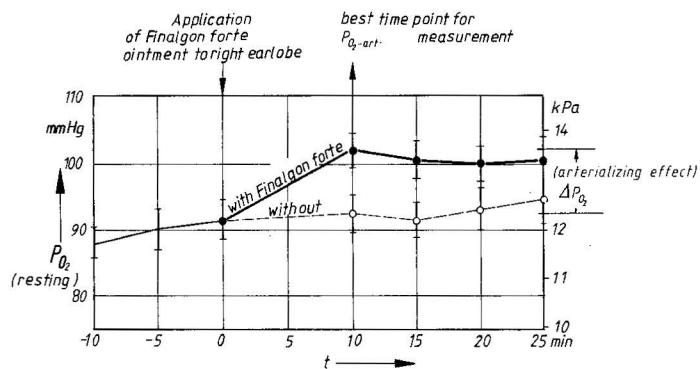


Fig. 198 Mean values and standard deviations of the resting P_{O_2} measured from blood samples taken from the right earlobe before and after "arterialization" by application of Finalgon® forte ointment to the earlobe. Simultaneous measurement without Finalgon® on the left earlobe of the same person; N = 6 [86]



Fig. 199 Universal P_{O_2} meter MO 10 (VE Kombinat Präcitronic, Dresden/DDR) with accessories, electrode system and hyperemizator. Development: Forschungsinstitut Manfred von Ardenne, Dresden/GDR. General representative: EMC-Erzeugnisse für Medizin und Chirurgie, D-5100 Aachen, FRG

1.1.5.3 the difficulties confronting the sufficiently representative determining of the mixed central venous PO_2 (cf. Fig. 9 for the mixing of the venous blood from various organs). In the same paragraph it was also shown by comparison with blood samples centrally drawn with an indwelling catheter that, taking certain conditions into account, even the blood taken from the non-ligated vena cubitalis provides sufficiently representative values of PO_{2-ven} at rest (cf. Fig. 14) [51].

The determination of the PO_2 is usually accomplished electrochemically using a galvanic cell that consists of a Pt/glass electrode, an electrolyte and an Ag/AgCl chloride reference electrode. The complete measuring device consists of the PO_2 micromasuring chamber, an amplifier, a microtonometer and a thermostat. The details of calibration and measurement with

this GDR standard system are fully described in [308]. The further development of this system to a simple PO_2 meter with electrically thermostatted micromasuring chamber MMK1F and measuring amplifier M65F (Metra, Radebeul, GDR) has also proved to be a rational way of carrying out serial measurements. By contrast to the complicated systems for blood gas analysis (for 3 parameters), this device specializes in PO_2 measurement and is therefore economically adapted to the requirements of the O_2MT .

This is particularly true of the new universal PO_2 meter MO 10 (Praecitronic, Dresden, GDR). The main field of application of this device (Fig. 199) is the accurate measurement of the PO_2 values using the invasive method with small blood samples taken from the hyperemized earlobe and from the vena cubitalis, respectively. Figure 200 shows a further view of

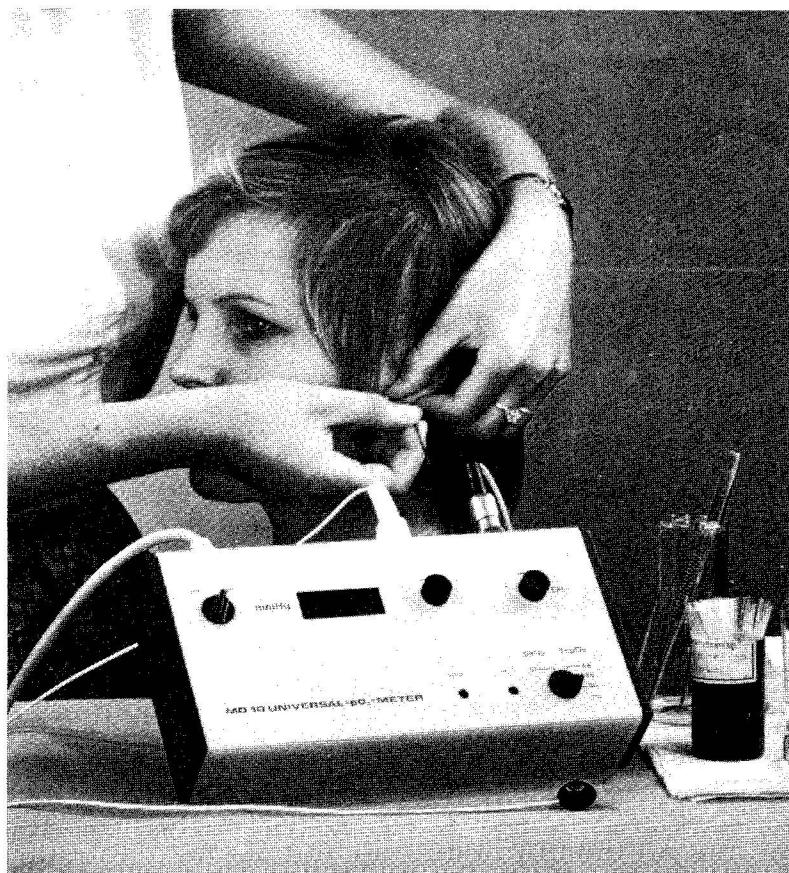


Fig. 200 The simple universal PO_2 meter MO 10 for the accurate measurement of the arterial and the venous peripheral PO_2 in blood droplets taken from the "arterialized" earlobe or from the vena cubitalis (no tourniquet!). Joint development: Forschungsinstitut Manfred von Ardenne and VE Kombinat Präcitronic Dresden/GDR. General representative: EMC-Erzeugnisse für Medizin und Chirurgie, D-5100 Aachen, FRG

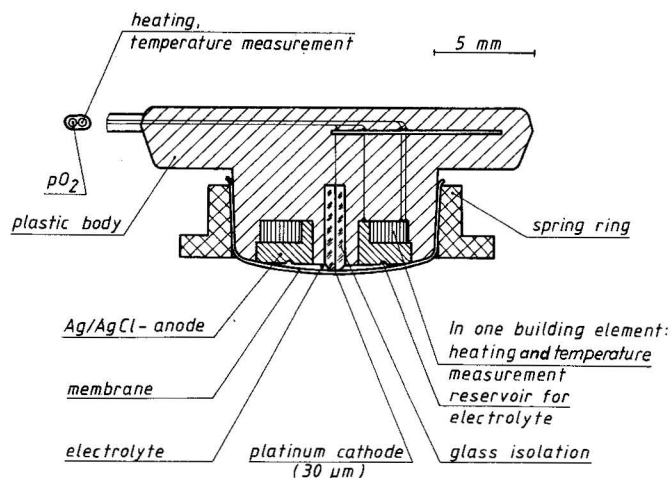


Fig. 201 Electrode systems of the universal P_{O_2} meter MO 10 (VE Kombinat Präcitronic, Dresden, GDR) suitable for measurement of $P_{O_{2-art}}$ and $P_{O_{2-ven}}$ from blood droplets, as well as transcutaneous determining of P_{O_2} courses. Development: Manfred von Ardenne Research Institute

this simple special device in action. In the background the blood sample is being taken from the earlobe. The basic device of the universal P_{O_2} meter consists of the measuring amplifier with digital display, and electronics for temperature control. The main element is the thermostatted electrode system, shown in Fig. 201, where the blood sample (one drop) is placed centrally for P_{O_2} measurement at 37°C. This electrode can be used if necessary for transcutaneous measurements at 44–46°C. The special feature of this electrode is its integrated heating and temperature measuring unit [320]. The device also has a hyperemizator, as in Fig. 202, to make $P_{O_{2-art}}$ measurements possible in cases where the "chemical arterialization" is not expedient or is not effective, i.e. in cases where, for example, several registrations must be made in the course of one hour. To measure P_{O_2} profiles transcutaneously, the device also has a socket for a recording system. A kit of chemicals, a mounting aid, and a larger set of prepared membranes are included as accessories. The standing time of the electrode system in permanent application is approximately one week, after which the electrode membrane must be replaced. Finally the accessories include an earclip which holds the hyperemizator (Fig. 202) or, alternatively, the electrode system with the same geometry. Due to the measurements in Figs 203 and 204 we attached importance to the option of the earlobe as a site of transcutaneous P_{O_2} measurement. These figures illustrate variation and systematic deviation of the measured values from the "true" P_{O_2} , when different sites and methods were chosen.

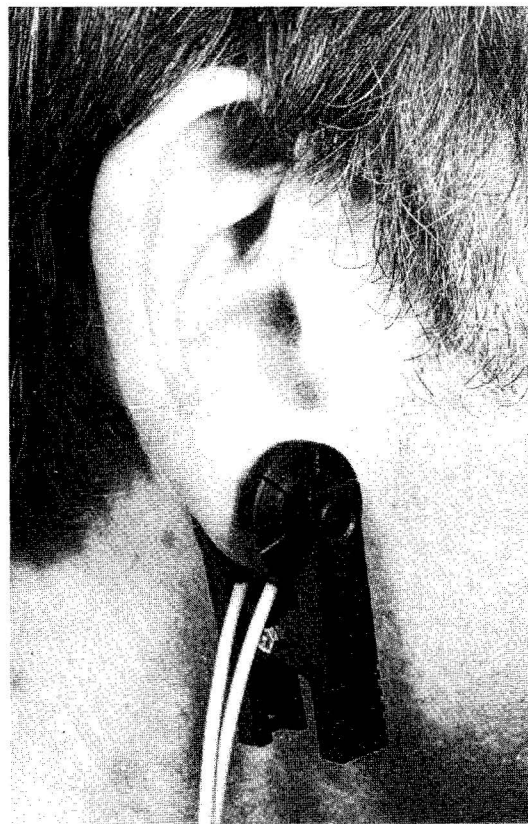


Fig. 202 Clipping the hyperemizator (accessory of the Universal P_{O_2} meter MO 10) onto the earlobe for continuous recording of $P_{O_{2-art}}$

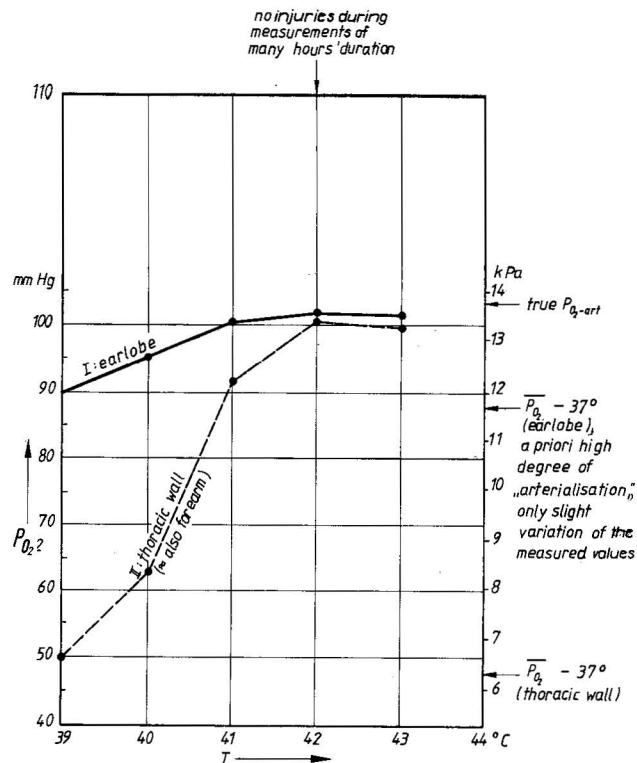


Fig. 203 Examples showing the dependence of the measured resting P_{O_2} on the skin temperature T . Thermal “arterialization” in the measurement from the earlobe (I) and the depilated thoracic wall (II). Only slight mean variation of the measurements from the earlobe

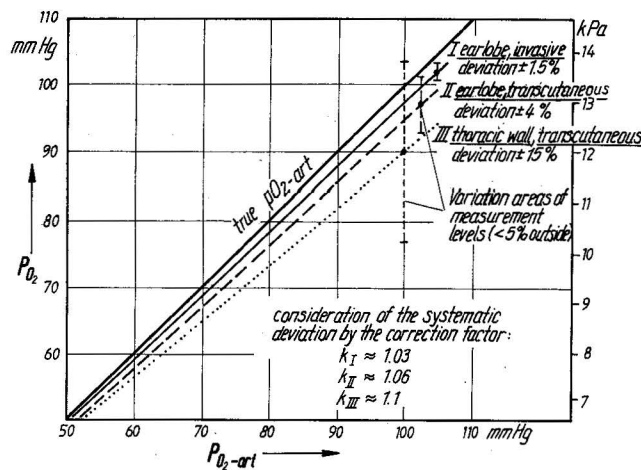


Fig. 204 Variation and approximate deviation from the true P_{O_2-art} of different measuring procedures: from blood of the hyperemized earlobe (I), by transcutaneous measurement from the earlobe (II), from the depilated thoracic wall (III) or from the forearm

The important thing in the O_2MT is generally to record changes in both P_{O_2} values as precisely as possible. This is why the invasive method using small blood samples from both the hyperemized earlobe and the non-ligated cubital vein is to be given preference. Surprisingly, a correct result is gained by simply placing a blood droplet in the centre of the electrode membrane. It can be concluded from this that the O_2 diffusion from the atmospheric air into the drop remains small enough in the manipulation time of up to 3 min, not to cause any distortion of the measured value. The blood sample itself is protected in the capillary

against an exchange of gases up to the delivery of the droplet. The interval should not be extended to above 5 min, however.

The application of the universal P_{O_2} meter for the transcutaneous large-area measurement of P_{O_2-art} , where required [320], is illustrated in Fig. 205. The less accurate but noninvasive method is indicated for permanent checking (trend measurements, detection of the quality of the vascular system, monitoring of the patient with triggering of an alarm, e.g. if the level falls below a lower limit as a result of heart or respiratory failure [313].



Fig. 205 Transcutaneous PO_{2-art} measurement with the earclip electrode system. Universal PO_2 meter MO 10

Transcutaneous PO_2 measurement was greatly developed by Lübbers and his school [162, 310, 311, 313, 315, 321]. Devices of this type with in-built registration systems have been put on the market by Draeger (Lübeck, FRG) under the name "Oxymeter" or by Hellige (Freiburg, FRG) under the name of "Oxymonitor", and by Roche (Basle, Switzerland) under the name of "Cutaneous PO_2 Monitor 630". In connection with this we should also mention the large devices for blood gas analysis in accordance with Astrup, which were first brought out by Radiometer (Copenhagen, Denmark) and AVL (Graz, Austria).

The working principle of the electrode for the transcutaneous large-area measurement of the arterial or tissue PO_2 in accordance with [313] is shown in Fig. 206. Figure 207 shows a cross-section of the assigned electrode system. This system exploits the known physical phenomenon that all resistance vessels of the skin (cf. Fig. 144) are dilated when a temperature of

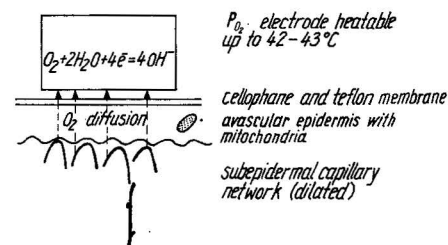


Fig. 206 Principle of the transcutaneous large-area measurement of the arterial PO_2 [313]

42–43 °C is reached. The circulation of the skin then increases by a factor of up to 36 (cf. Fig. 141). With this high degree of hyperemization the PO_2 of the capillary blood comes close to that of the arterial PO_2 . This is reflected by the fact that, with moderate reduction of the capillary circulation due to the constriction of nutritive vessels, the PO_2 initially remains con-

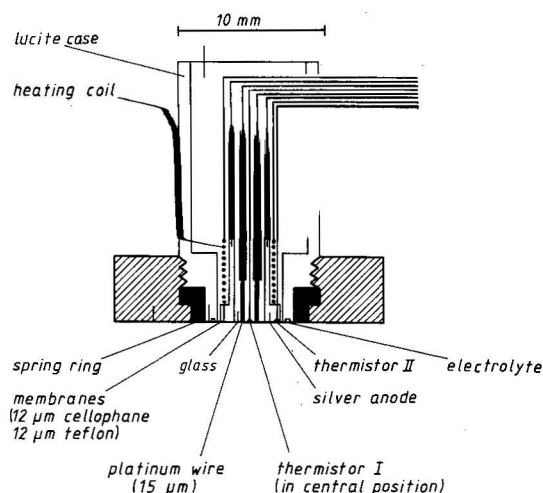


Fig. 207 Heatable measurement system for the transcutaneous large-area measurement of the arterial PO_2 . Setting time ≤ 30 s [313]

stant in this area. The oxygen diffuses from the upper capillary layer to the PO_2 electrode of the Clark type, fixed to the skin. The hyperemia is attained here by the heating of the electrode via the silver anode. For this a nickel-tungsten heating wire, the temperature of which is regulated at 43°C by a thermistor placed close to the surface, is inserted into the silver anode (Fig. 207). The PO_2 measurement is carried out with three platinum cathodes, sealed in glass, each with a diameter of only $15\ \mu\text{m}$ and with individual contact to the skin surface. They are switched separately in opposing connection with the silver reference elec-

trode. Two of the reduction currents are normally recorded. Their agreement is a good check that the electrode is placed correctly on the skin surface. In more recent designs the three electrodes are connected parallel.

A nomogram for the exact calibration of the discussed PO_2 meters with atmospheric air at a given barometric pressure is given in Fig. 208.

Finally, a non-invasive colorimetric method of PO_2 determination using "arterialized" capillary blood (e.g. earlobe) should also be mentioned. With this method the color of the red blood cells, which is dependent on their O_2 saturation, is determined transcutaneously with sufficient accuracy using an electronic multispectral photometer [316]. The Ohmeda Biox III Oximeter (Schubart, Wiesbaden, FRG) is a modern device of this type. This method need not be considered for the measurement of the $PO_{2\text{-art}}$ as it becomes very inaccurate at levels of 90 mmHg (12 kPa), which must be determined exactly for the work undertaken here. It could, however, become important in future for the noninvasive measurement of the $PO_{2\text{-ven at rest}}$. One obstacle involved in this method, namely the disturbance of the value to be measured by arterial capillary blood flow in the upper skin layers, has been overcome by developments in our Institute. The simple trick lays in squeezing the blood out of the microvessels in the small area involved in the measurement procedure.

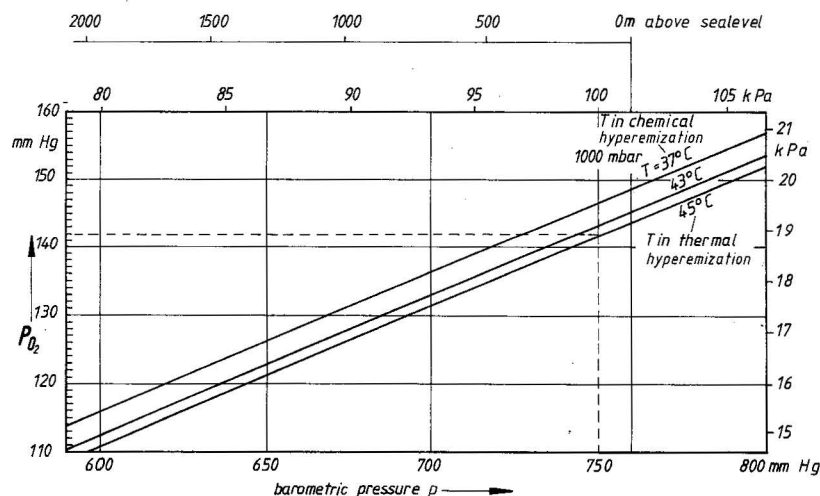


Fig. 208 Oxygen partial pressure in air at 100% relative humidity dependent on barometric pressure p and temperature T . Auxiliary table for calibration of PO_2 measurement instruments

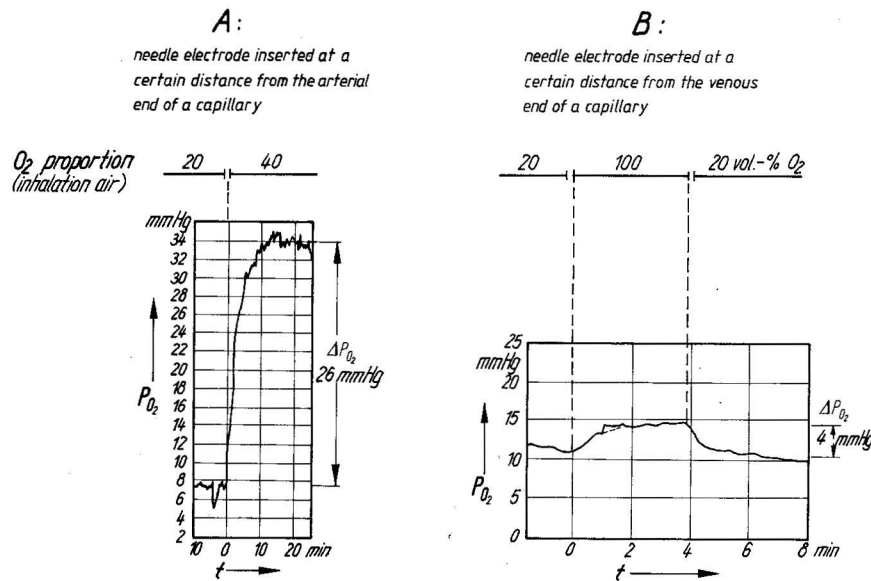


Fig. 209 Direct P_{O_2} recordings using a microelectrode inserted in a poorly perfused tissue area (A, near the nourishing arterial end; B, near the venous capillary end) after a sudden increase of the O_2 proportion in the inhalation air [304]. Cf. also Figs. 97 and 192. The absolute P_{O_2} values are not exact due to different diffusion fields around the electrode during calibration and measurement

3.4.3 Results of P_{O_2} measurements in living tissue

Of the large range of experimental results accumulated we will give here only such P_{O_2} measurements as can either count as classic examples or give information on the effect of the O_2 MT or its individual steps.

Micro-area P_{O_2} registrations in tissue with poor blood supply after sudden increase in the proportion of oxygen in the inhalation air are given in Fig. 209. On the basis of [163, 272] we can conclude from the fact that in both registrations the increased P_{O_2} level did not become constant before a certain time-lag of some minutes, that in both cases the microelectrodes were placed at a greater distance from the nutritive capillary (larger time constant O_2 - τ_A in the tissue). The same conclusion can be drawn from the relatively low initial P_{O_2} levels. It is interesting that in example A an increase of 26 mmHg occurs in the tissue, when the proportion of O_2 in the inhalation air is elevated to 40%, whereas in example B an increase of only 4 mmHg is seen, even when pure oxygen is inhaled. This great difference in the P_{O_2} gain indicates that in A the microelectrode was inserted near the arterial end of the capillary, and in B near the venous end. In connection with this we refer the reader to Figs 97

and 192 above. [304] reports on the determination of P_{O_2} distribution curves in the tissue (P_{O_2} histograms) by means of multiple micro-area measurement with an eightfold P_{O_2} electrode system. It also shows for the first time the influence of the level of the P_{O_2} -art on the P_{O_2} histograms under physiological and pathological conditions (e.g. recording of induced disorders of the microcirculation).

A microarea P_{O_2} measurement made during the implementation of the 1st and 2nd steps of the O_2 MT with a microelectrode inserted into a tissue site with initial oxygen deficiency is given in Fig. 210. It shows considerable increases in the P_{O_2} level at the site of measurement both after oral administration of drugs to improve O_2 utilization (1st step) and after doubling the O_2 content of the inhalation air (2nd step). This example shows concretely how O_2 deficiency existing in the intercapillary space is eliminated during O_2 MT.

The measurement of the P_{O_2} -art under conditions of rest allows an assessment in the individual case of the extent to which the O_2 offer in the walls of the arteries or arterioles rises and to which the O_2 delivery to the tissue is in-

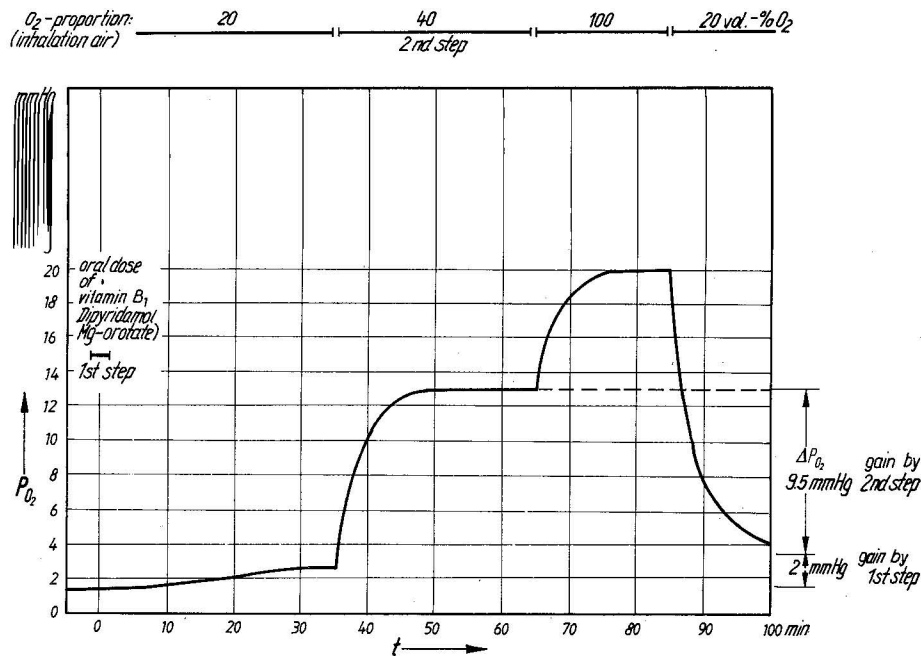


Fig. 210 PO_2 micromasurement with needle electrode in a tissue area with initial O_2 deficiency (at $t = 0$ min) followed by the 1st and 2nd steps of the O_2 MT. Re-drawn registration of a rat experiment [303]. Measurements of this kind give no direct information about the gain in O_2 metabolism

creased due to the increase in the PO_2 of the inhalation air. The frequency distribution of the resting PO_{2-art} , according to determinations in our Institute between 1977 and 1982, given in Fig. 211, gives an impression of the conditions in nontreated volunteers of all age groups. With patients having values of PO_{2-art} 70 mmHg (9.3 kPa) or a low utilization factor η ($< 18-20\%$), for whom the O_2 MT is particularly indicated, it is very important to use therapy variants which can contribute to the improvement of their weakened state by moderate exertion.

In the treatment of circulatory disorders in the extremities, large-area PO_2 measurements can give quantitative indications as to the mean tissue PO_2 before and after treatment. The significance of such measurements can be increased by combining them with determinations of the local tissue temperature.

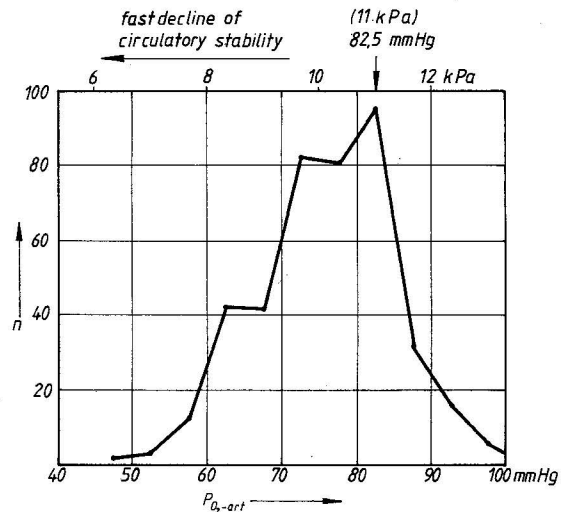


Fig. 211 Frequency distribution of the arterial PO_2 in 411 untreated volunteers of both sexes and of all age groups (measured invasively under resting conditions). M. von Ardenne Research Institute 1977/82

3.4.4 Transcutaneous measurement of the tissue PO_2 , dependent on blood flow, after a ligature. Determination of the quality of the vascular system

The transcutaneous determination of the course of tissue PO_2 during blood flow inhibition and after lifting the occlusion represents a special case in PO_2 measurements in living tissue [323, 324]. Typical examples are given in Fig. 212.

The angles of inclination α_1 (after clamping the blood flow) and α_2 (after restoration of the flow), easily and non-invasively determinable in routine practice using devices as shown in Fig. 205, are of high diagnostic value. The temporal

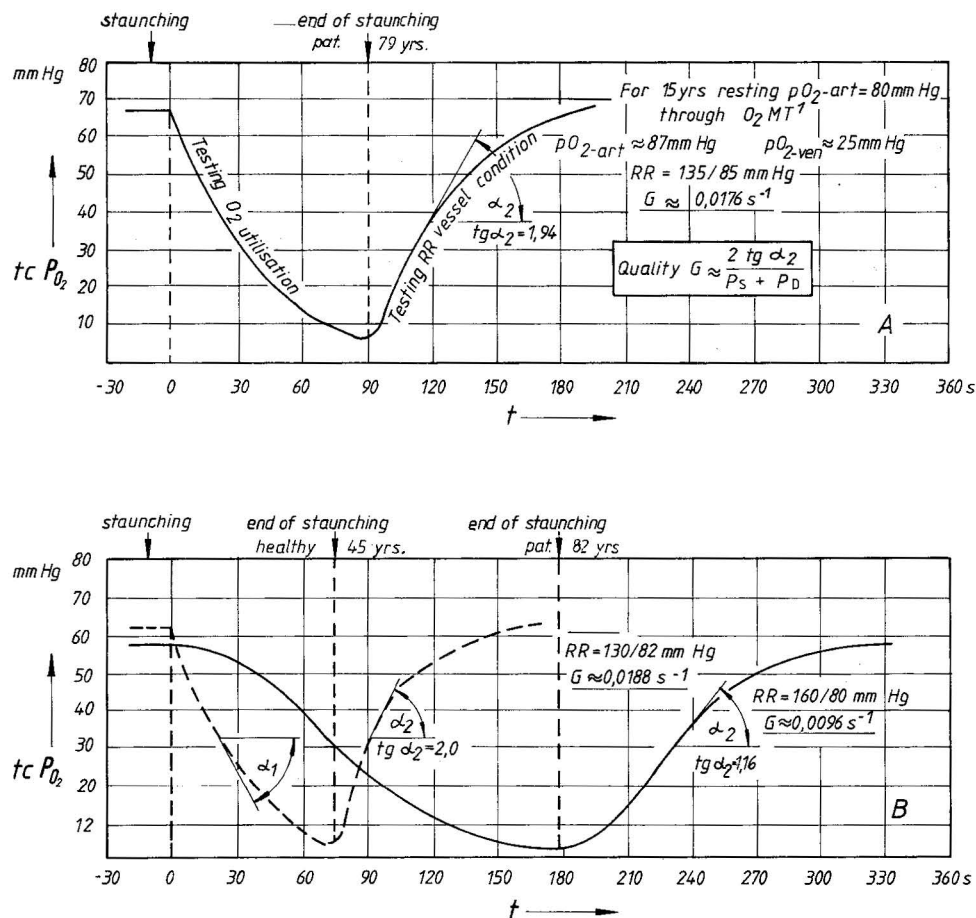


Fig. 212 Course of the transcutaneous (tc) P_{O_2} measured in the underarm during blood stanching in the upper arm by means of a cuff and after lifting the compression in a 79-year-old male subject in whom the O_2 status had been held high for 15 years by $O_2 MT$ (A) and in a male patient of 82 years without $O_2 MT$ treatment (B). P_s, P_d = systol. and diastol. blood pressure values (RR). For comparison, the curve of a healthy 45-year-old male is included below (broken line). Method to achieve diagnostic characteristic values for O_2 utilization in tissue and for quality of the vascular system

¹ Prevention of arteriosclerosis

course of the drop in the transcutaneously measured tissue P_{O_2} during the inhibition allows us to draw conclusions about the extent and dynamics of the O_2 utilization in the tissue. Furthermore, the quality Q of the vascular system is reflected in the re-increase in the tissue P_{O_2} after lifting the occlusion, and in the easily determinable mean value of the (RR) blood pressure $\frac{P_s + P_d}{2}$, as is shown for an arm in Fig.

205. At present there are only a few reports in literature about the results gained with this

method. The age dependency of the characteristic values α_1, α_2 and Q must be further investigated.

This method was applied in our Institute to gain further objective data for the effect of the $O_2 MT$ in 30 volunteers, especially in their vascular system, before and after the 36 h $O_2 MT$ procedure GK 4-I (with 18 sessions). With reference to the drop in the tissue P_{O_2} during the blood flow inhibition, a significant reduction in the variation of α_1 (i.e. normalization) was observed as a consequence of the

O₂MT. In the same patients under study there was a *greatly increased steepness of the angle α_2* , especially in individuals with poor initial α_2 values. In 20% of the cases examined improve-

ments in the α_2 to roughly twice the initial value were measured. The main effects did not usually occur after a single treatment cycle, however, but only after several repetitions over years.

A relative characteristic value for the (local) quality Q of the vascular system can be gained from α_2 by means of the *joint measurement or both RR blood pressure values p_s and p_d* (e.g. immediately afterwards), resulting in the relation

$$Q = \frac{2 \cdot \operatorname{tg} \alpha_2}{p_s + p_d}$$

Thus there is a diagnostic method available for routine use, in order to recognize arteriosclerotic damage in the vascular system.

The curve in Fig. 212 A represents the first measurement along these lines in an *old volunteer (79 years, author's self-experiment)*, who had for 15 years almost without interruptions, ensured a resting PO_{2-art} of ≥ 80 mmHg (10.6 kPa), by the optimal application of the O₂MT. The course registered is only slightly less favorable than that for a normal 45-year-old person, included in Fig. 212 B for comparison. The curve indicates an exceptionally good condition of the measured blood vessel. This result can probably be seen as first evidence of the correctness of our hypothesis, explained in Paragraph 5.5.2, that *the development of arteriosclerosis can be greatly delayed by main-*

taining the O₂ status, especially the PO_{2-art} at a high level without interruptions, if possible. These conditions even make possible the reversal of early stages of arteriosclerosis, as is shown

by detection of the increased quality of the vascular system and of the enduring drop in the RR values in hypertensive persons after a good O₂ status has been maintained by O₂MT for several months.

The author applied the same, non-invasive method in the lower extremities by compression of the *arteria femoralis* (on the upper thigh, using a larger sphygmomanometer for greater counter-pressure) and on the lower thigh just below the knee [325]. This procedure is contraindicated when the patient has varicose veins. With only a moderate increase in effort, these investigations result in objective data demonstrating the improvement of the flow parameters in the legs by means of variants of the O₂MT, with and without HOT*-UVR treatments, as further characteristic values of the stage of the arteriosclerotic degeneration of the vascular system, and in patients suffering from intermittent claudication (especially diabetics). This simple method can also be used to diagnose the approach of critical vascular states in the lower extremities from transcutaneous PO_2 measurements on the instep¹, so early that counter-measures (O₂MT, HOT*-UVR, drugs) can be initiated whilst the disorder is still reversible.

¹ Electrode well secured by two-sided adhesive tape. PO_2 levels obtained are lower than in the arm

3.4.5 Taking point measurements of the PO_2 and of other parameters from the visual field of a vital microscope with color video. Spirometric systems

The etiology, diagnosis and therapy of many diseases are increasingly being promoted by the more recent research into microcirculation. The significance of an almost *punctiform measurement of PO_2 and glucose concentration c_{glu}* in the *capillary bed of tissues* therefore needs no explanation. What mattered in our research was to check the PO_2 , e.g. the maintenance of anaerobic experimental conditions (and the study of their consequences), and to measure the extravasation of glucose under different conditions, e.g. at a certain temperature, in a vital microscopic array.

Glucose concentration in the terminal vascular bed has not yet been measured with micro-

electrodes; the PO_2 virtually only with needle electrodes. Reitnauer and the author have developed a method of measuring both values (without needle electrodes or micromanipulators) paravascularly with *controlled variation of the environmental conditions under a vital microscope with video recording* [327, 328].

Figure 213 shows a *schematic diagram of the microscope stage unit* for the point measurement of the PO_2 and c_{glu} . The device with vital microscope, its accessories and color TV camera during an experiment are shown in Fig. 214. The overview (Fig. 215) shows the *complete system with video recorder and color TV receiver*.

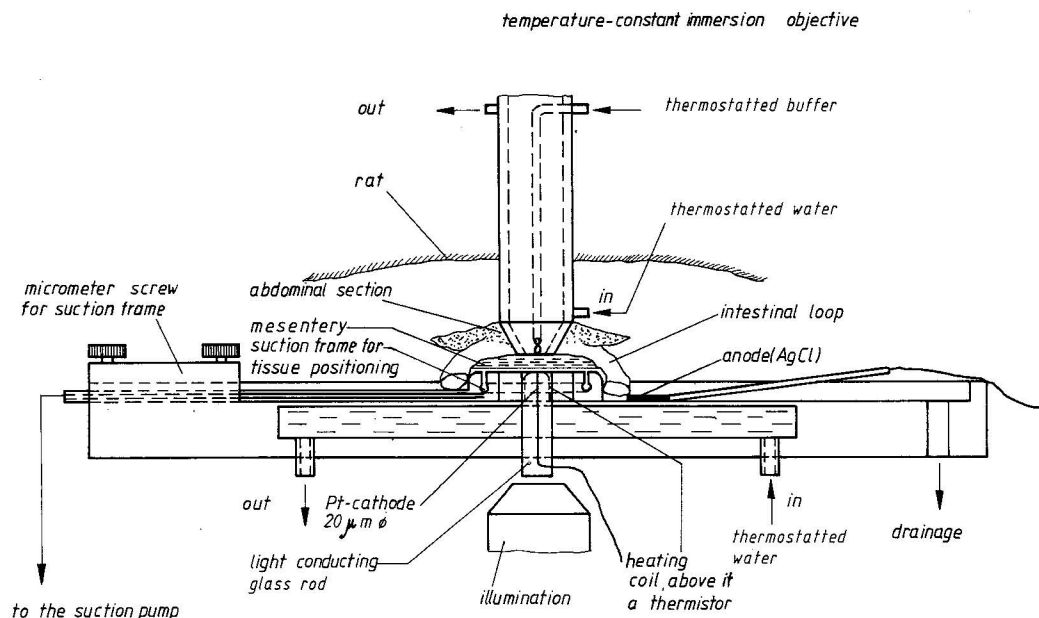


Fig. 213 Schematic presentation of the vital microscopic equipment with light-conducting P_{O_2} electrode for the measurement of P_{O_2} in the area of microcirculation of the mesentery of a rat

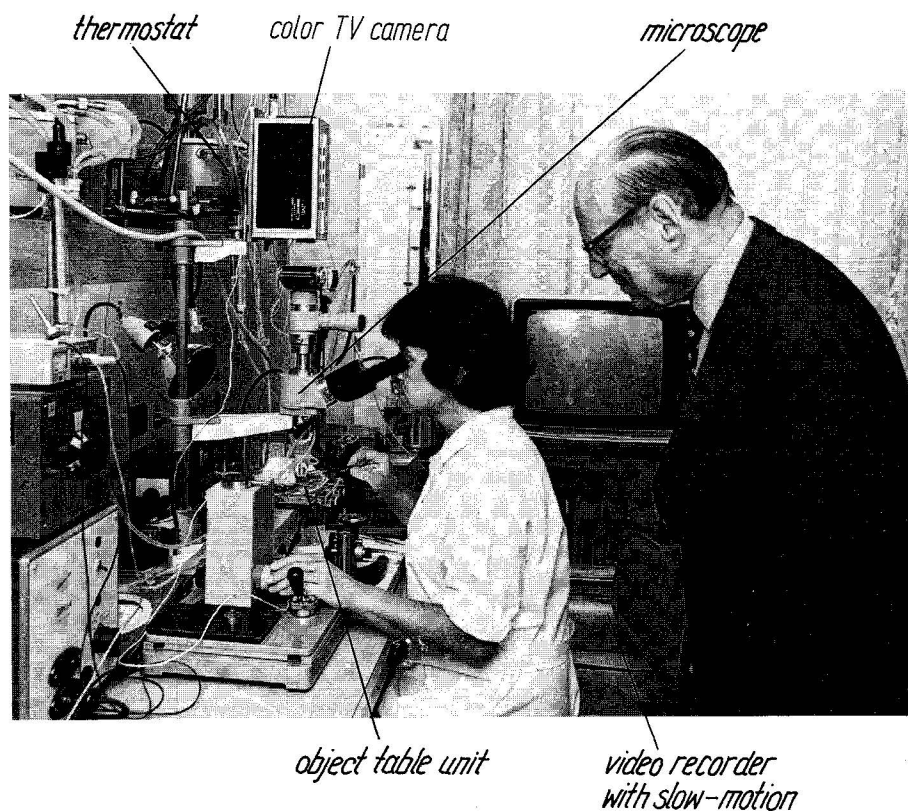


Fig. 214 Partial view of the color video vital microscopic equipment

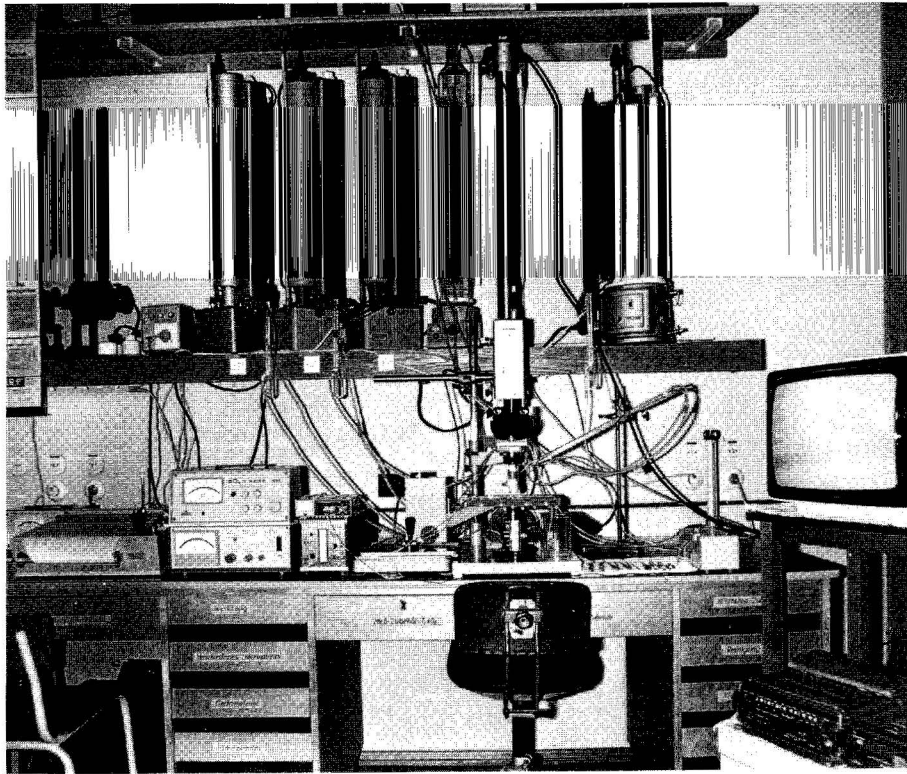


Fig. 215 Overview picture of the vital microscopic equipment (color video) in the Manfred von Ardenne Research Institute. On the rack (from left to right): over-heating protector for the thermostats; thermostats for constant 37, 43 and 45 °C; vessel containing sprinkling fluid; camera stand; thermostat for different temperatures. On the bench (from left to right): object temperature recorder; gauges for P_{O_2} measurements; adjustable electrical heating unit for the microscope table and the sprinkling fluid; manipulator; microscope with video camera and P_{O_2} meter for sprinkling fluid; surgical instruments, flowmeter, and monitor with video recorder. For the simulation of the conditions in solid tumors, a special measurement chamber is envisaged, which makes possible the observation of the microcirculation under O_2 deficient or anaerobic conditions

One advantage of the style of construction described is that it enables us to measure even with very short working distances, because no micromanipulators are necessary between the lens and the object. As can be seen from the schematic diagram, the measuring system consists of a light-conducting glass rod inserted in the microscopic stage, which contains in its center the *platinum cathode* ($d = 20 \mu m$). A chlorinated silver wire ($d = 0.3 \text{ mm}$) wound round this rod represents the anode. At the top the electrode rod is surrounded by a case. The ring slot thus formed is filled with an electrolyte, the whole system covered by a teflon membrane (Clark type electrode). If the glucose concentration is to be measured, an additional cellophane membrane is fixed over it, and glucose oxidase solution is placed between the two membranes. The tip of the Pt cathode is visible in the microscopic field as a dark spot. When the desired biological object (tissue sample, see below) is layered over the electrode, P_{O_2} or c_{glu} can be measured. The electrode system is calibrated before and after measure-

ment by being sprinkled with a solution of appropriate oxygen and glucose composition.

The mesenterium of Wistar rats was used as the *object of examination*. The animals were anesthetized with 1 g/kg ethyl urethane s.c. The microscopic observation was undertaken with a Leitz *saltwater immersion lens* SW 25/0.6 (tube factor 1.6x, ocular 8x), thermostatted to 37 °C. For the sprinkling fluid we used oxygen-free (N_2 -gassed) isotonic phosphate buffer (pH 7.4; addition of 1% dextran M 40; Serumwerk Bernburg, GDR), also warmed to 37 °C.

The system was calibrated by covering the electrode system (Pt cathode and AgCl anode) with 37 °C warm, air-saturated (maximum pointer deflection) or N_2 -gassed (reference value) sprinkling fluid. After partial coeliotomy of the animal along the linea alba, the animal was placed on the microscope stage, the mesenterium of a loop of the small intestine was gently lifted out and sprinkled with N_2 -gassed buffer. The microscope was adjusted so

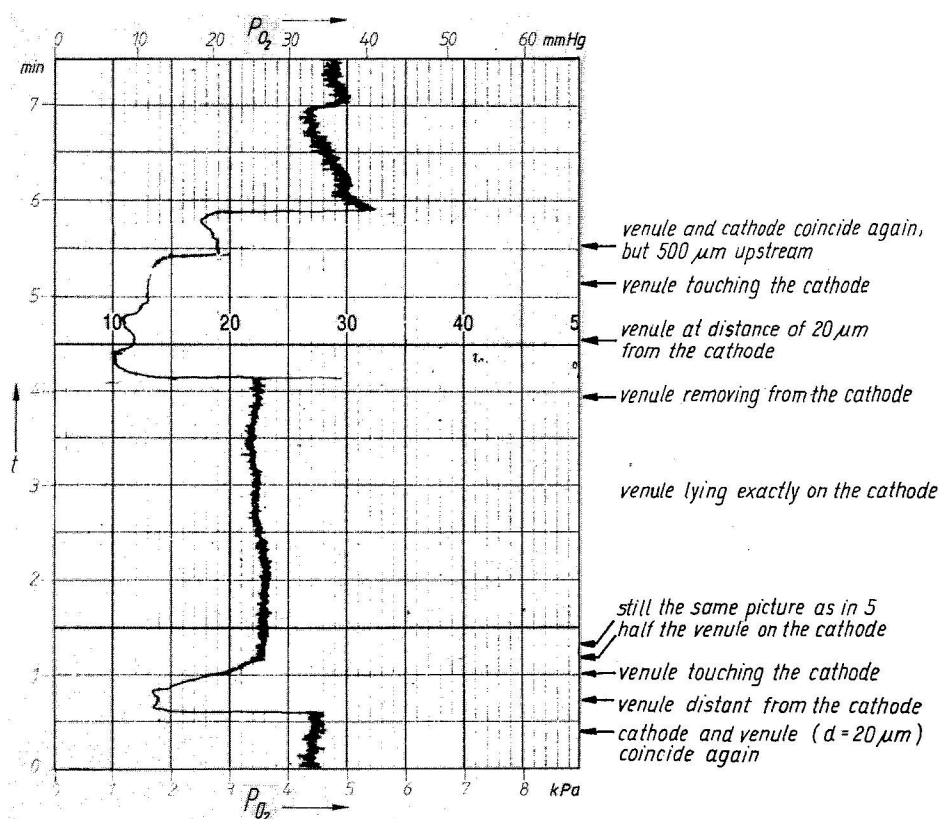


Fig. 216 Registration of the paravasal P_{O_2} of a venule in the rat mesentery rinsed with an N_2 gassed buffer solution

as to make the tip of the Pt electrode, on which the mesenterium lay, visible in the centre of the microscopic field. By careful shifting, any structure of the mesenterium (arterioles, capillaries, venules and avascular areas) could be made to coincide with the cathode.

The described arrangement makes possible simple para- or interval P_{O_2} measurement at the respective tissue structures covering the cathode tip. On average we gained the following paravasal P_{O_2} levels: around arterioles ($d = 20\text{--}30\ \mu\text{m}$) 65 (range 63–66) mmHg; around capillaries ($d = 7\text{--}20\ \mu\text{m}$) 51 (36–60) mmHg; and around venules ($d = 20\text{--}40\ \mu\text{m}$) 41 (25–48) mmHg. The mean arteriovenous P_{O_2} difference was 24 mmHg (3.2 kPa). The records in Figs 216 and 217 show some examples.

It was also confirmed that the paravasal P_{O_2} , under otherwise constant conditions, is a *highly sensitive indicator of every change in the blood flow velocity*. With a spontaneous standstill in blood flow the oxygen level sank towards zero

within a few minutes. We also occluded individual vessels using a micromanipulator and glass microneedles, and here, too, we measured a corresponding drop in P_{O_2} . With this system we could examine *pore formation and plasma extravasation* in capillary areas with lowered pH, after i.v. administration of fluorescent dyes, e.g. sodium fluoresceinate, using an ultra-violet microscope.

This paragraph has dealt in depth with methodological studies, because the difficult measurement problems described here demand the *greatest experimental skill* and because the *methodological procedure represents a kind of classic example*. The content of this paragraph could perhaps also mean that sceptical comments on bioelectronic measurement of our working-team, such as those in [329], will no longer be made in future.

The counterpart of the research into the micro-processes with this system in our Institute is the research into the overall effects of the different

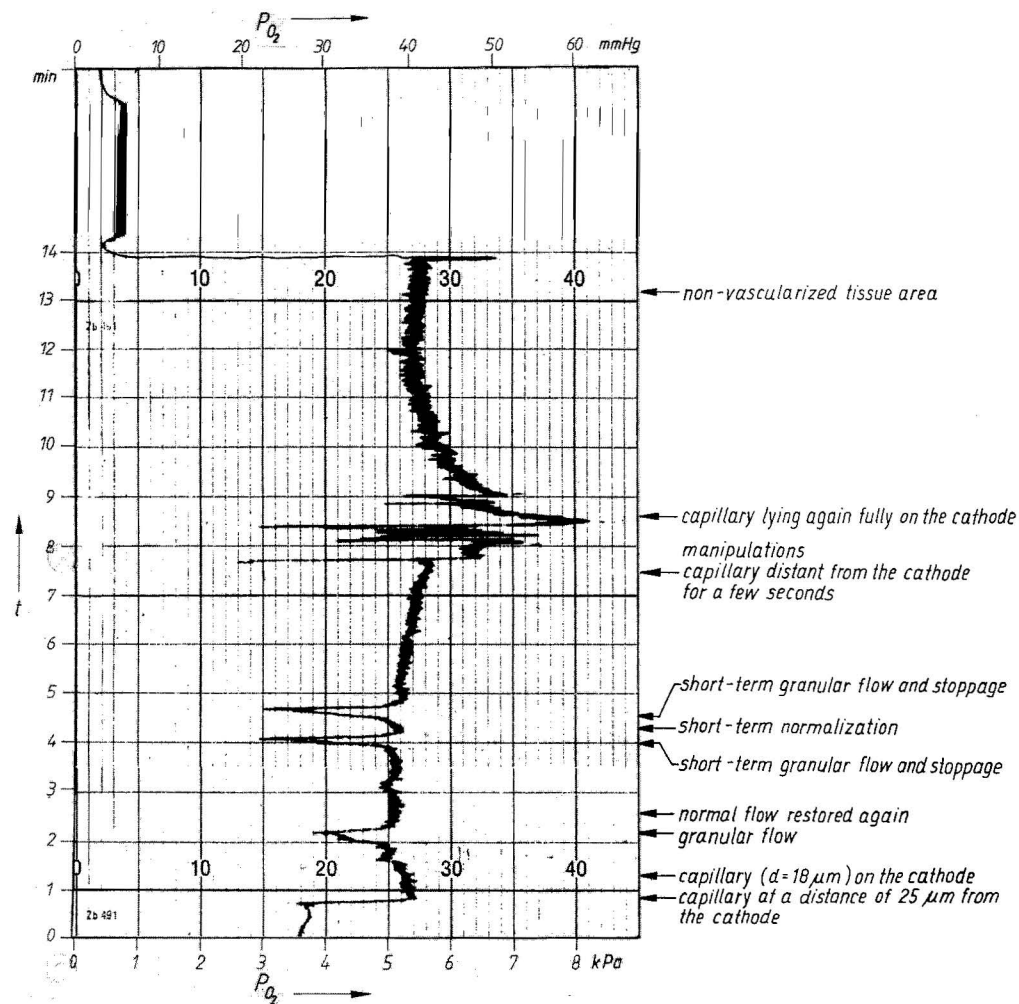


Fig. 217 Registration of the paravasal PO_2 of a capillary in the rat mesentery rinsed with an oxygen-free buffer solution. Even bloodflow changes lasting just a few seconds are shown in the PO_2 curve

variants of the O_2 MT in sick and healthy individuals by means of the direct spirometric measurement of the O_2 uptake and CO_2 production under resting conditions, with the computerized Hellige Oxycon 4 system (Hellige, Freiburg, FRG), including data printer. The comparison of the documentations made before and after O_2 MT in an already high but constantly further increasing number of debilitated patients resulted in lasting overall gains, as follows:

with the increase in the HbO_2 saturation difference	to 233 %,
there occurred a rise in the O_2 uptake at rest	to 150 %,
and an increase in the CO_2 production at rest	to 170 %,
The respiratory quotient RQ rose from 0.83	to 0.91–0.93.

(For a print-out as a single example of this, see Appendix)

These findings are further evidence of the general switching effect of the blood micro-circulation, discussed at the start of this book. Assuming that the generation of energy-rich phosphates (ATP, CP) in the organism is roughly proportional to the CO_2 production, at rest, these results mean that the *energy situation of the human organism can be lastingly improved* (in responders) *by oxygen multistep therapy in a surprisingly high percentage of cases*. This is a result which, due to the central importance of energy for almost all mechanisms of prevention, prophylaxis, therapy and defense, should be of great significance for medicine and the Health System of the future.

In connection with this we would refer the reader back to Fig. 66. The expected levels of the O_2 uptake, under resting conditions, for healthy persons dependent on age can be taken with good accuracy from the solid line there

(standard conditions). The position of the point of measurement in this figure characterizes the momentary energetic or health status. When a large number of data obtained from weakened individuals in need of therapy were included in this diagram, it was found that nearly all values measured before O_2MT were below the ex-

pected values, but almost all values obtained after O_2MT were significantly higher. This result confirms the findings in weakened patients at a sanatorium, shown in Fig. 18, and obtained from the measurement of the resting levels of PO_{2-art} and PO_{2-ven} under inexpensive routine conditions.

4. Variants of the oxygen multistep therapy

4.1 Overview and common aspects

At present there already exist *numerous procedural variants of the O₂MT*. It is the aim and effect of nearly all variants that the *blood microcirculation is "highly charged" over a period of months up to years*. They are therefore designed, on the basis of measurements on many hundreds of volunteers, in terms of type, administration and timing of the steps, in such a way that the probability is high that in the individual patient case the bioenergetic triggering of the discovered cellular capillary wall switching mechanism with dilation of the narrowest capillary cross-sections will take place. The procedural variants differ from one another mainly in the *type, in the administration and in the timing of the 3rd step*, which determines the strength of the circulation, especially the cardiac output (COP). *Quick procedures or short procedures* result when the COP is temporarily increased by physical exertion or by stimulating drugs, as explained in Paragraph 1.1.10. However, these variants cannot usually replace the 36 h O₂MT (standard) procedure. Some variants allow for the combination of procedures and combination with additional steps (e.g. with the HOT*-UVR method) to intensify the effect. This great variety enables the medical practitioner to *adapt the therapy to the individual patient to a large extent*. This important role of the doctor requires him to have an overview of the scientific foundations of all measures and combination of measures used in the O₂MT. The physiological and technical details have been presented in the previous chapters of this book in order to help here. For the same reason Table 23 gives an *overview of the different procedural variants of the O₂MT and the oxygen multistep immunostimulation (O₂MI)*. See Appendix for the most recent 5x20 min O₂MT short procedure, GK 3-I.

The relation to the strength of the effect, i.e. to the *certain crossing of the switching threshold of the capillary switching mechanism*, explained in Paragraph 1.1.1.2, applies to all procedural variants. It is absolutely essential for the restoration of a good O₂ supply to the endothelial

cells at the venous capillary end by means of diffusion, that *as high a level of the PO_{2-ven} as possible* is brought about during therapy. This is achieved by the generation of a high PO_{2-art} (high O₂ offer adjusted to the respiratory minute volume, RMV), and by a high capillary blood-flow $\dot{Q}$ (high COP, physical exertion, no implementation of the procedure during periods of circulatory weakness except in special emergency variants). The absolute level of the PO_{2-ven} and, when the procedure is fractionated, the time relation K of the procedure time (sum of the treatment hours) to the total duration of the procedure, determine the *total duration of treatment required*. For example, $K = 36 \text{ h}/432 \text{ h} = 0.0833$ for the 36 h 18 day (= 432 h) O₂MT procedure GK 4, and for the O₂MT quick procedure GK 2, without fractionation $K = 15 \text{ min}/15 \text{ min} = 1.0$. Since the value K considerably influences the amount of time and O₂ required for the respective variant, the notion of *time efficiency* and, in Paragraph 1.1.1.2, the notion of *efficiency exponent* was introduced. The influence of the time relation K can be explained by the fact that, in the usually considerable pauses between the individual sessions of treatment, the endothelial cells in the deficient zone at the venous capillary end swell up again slightly. The negative influence of longer pauses between the sessions (e.g. no treatments at weekends) was also reflected in measurements of the PO₂ at rest. The timing of the procedure should theoretically be so designed that as little time as possible remains for a retumescence of the endothelial cells (especially in the first phase of treatment before the switching threshold has been reached). This instruction can only be followed up to a certain extent, however, because other considerations (physical disablement, no stress capacity) force a compromise in the question of "time efficiency".

The recommended programming of the different variants is given in this section of the book in the framework of a unified basic scheme, with details of the type, administration and temporal organization of the individual steps.

This section therefore refers mainly to the practical researcher, the doctor and his patient. The great differences in the 15 procedural variants (Table 23) allow the treatment to be largely adapted to the situation in the individual case. All treatments should be undertaken exactly according to the programming tables of the variants, and no further steps should normally be added, in the interests of the results and their comparability. Unauthorized modifications are also not permissible due to the decline in the effect to be expected. This also applies to the too frequent repetition of procedures which, in the 15 min procedure, for example, can cause the toxic O_2 -flow limit to be approached. The logical conclusion of these words is that the oxygen multistep treatment should always be carried out (or, in the case of procedure repetitions in the patients' home, begun) under the observation and guidance of a doctor experienced in O_2 MT.

In most procedural variants, success depends to a very great extent on the numerical value of the PO_{2-art} measured in the patient during O_2 -inhalation (see also 1.1.1.2). This value should therefore always be measured shortly after the

start of the procedure, for prognosis and, if necessary, for adaptation of the procedure. Such control measurements also ensure that there are no methodological errors in the oxygen application (O_2 -flow too low, O_2 -applicator badly positioned, unsuitable applicator selected etc.). Measurements performed in the intervals between treatment phases are very informative, as they show the success as the rate of the increase in the PO_{2-art} , at rest, or of the η -value during the oxygen multistep procedure.

A very advantageous characteristic of almost all variants of the oxygen multistep therapy is that it can be performed non-invasively.

The O_2 MT procedures all have in common the fact that they are nearly natural and therefore have hardly any side-effects. They mainly stimulate, trigger off or positively influence natural processes.

There is a great difference between the *whole body variants* on the one hand, and the *body section variants* on the other. In the latter the "high-charging" of the blood microcirculation is only aimed for in a certain section of the body.

4.2 Whole body variants

4.2.1 Oxygen multistep sauna procedure GK 1

The programming of the O_2 MT sauna cure procedure is given in Table 24. A cure procedure with a lasting increase in the PO_{2-art} or of the O_2 uptake, and the reduction in the PO_{2-ven} , measured under resting conditions each, i.e. with a long-lasting improvement in the energetic or O_2 status of the patient's organism, is achieved simply by attending the O_2 MT sauna [84, 330–335] roughly 18 times. It is therefore recommended that the visit to the O_2 MT sauna be planned according to this table and that, at the end of the cure, the success of treatment be documented by the determination of the η -value or, even better, by the determination of the increase in the O_2 uptake, at rest.

The technical equipment of an exemplarily equipped O_2 MT sauna is shown in Figs 218 and 219.

Examples of indications for an O_2 MT sauna cure are [84, 332]:

1. Cardiovascular fitness training
2. System diseases of the connective tissue (joints and supporting apparatus)

3. General strengthening processes (immuno-stimulation, prophylaxis against infections)
4. Conditioning of the external respiratory apparatus
5. Local hypoxia (coronary, cerebral, renal, peripheral)
6. Failure of oxidative metabolic processes (chronic poisoning)
7. Myogelosis of various origin
8. Sleep disturbances
9. Reduction of probability of cancer in combination with daily administration of thymus preparations (cf. also Paragraph 5.3.13.4).

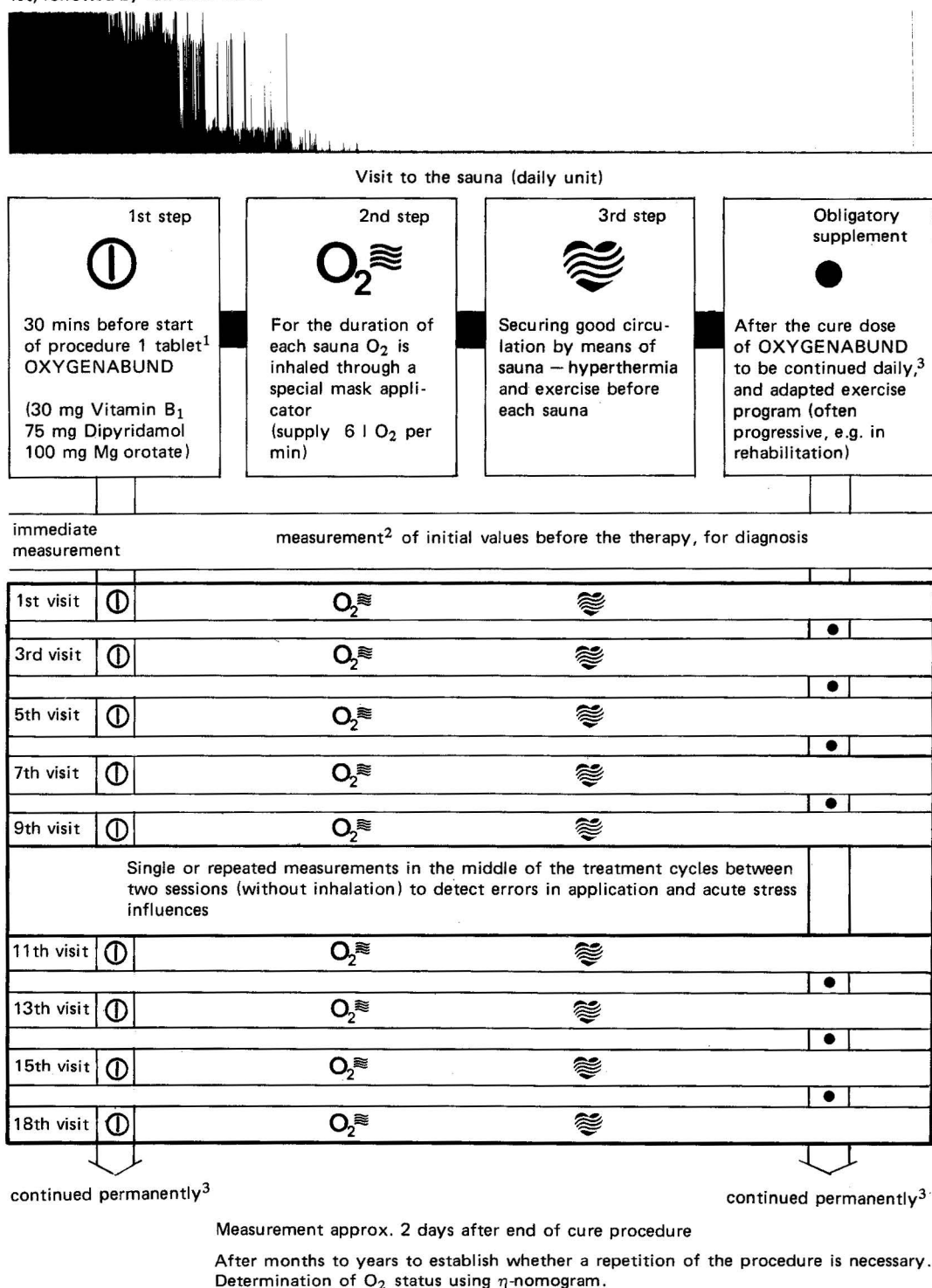
With the O_2 MT sauna, as with all variants with whole body hyperthermia, the great increase in the PO_{2-art} leads to an additional increase in effect, due to the O_2 -binding curve of the blood being shifted to the right after the increase in body temperature (cf. Fig. 8). It is striking that in patients with reduced circulatory reserves there is often a considerable drop in the PO_{2-art} with an increasing amount of time spent in a normal sauna. In healthy volunteers there is

Table 23 Process variants of Oxygen Multistep Therapy and Oxygen Multistep immunostimulation

Abbreviation	Description (total O ₂ requirements in l)	Additional steps	O ₂ flow (l/min ⁻¹)	General state of the patient	Main indications
1 GK 1	O ₂ multistep sauna procedure 18 saunas (1080–2160)	Footbaths 37 °C and 43 °C alternately. Two baths of 10–20 min. Finally plunge bath at 18 °C	6 Special mask applicator	Sound heart, also older people (light hyper- thermia)	Combatting effects of distress Stabilization of circula- tion
2 GK 2-I	15 min O ₂ multistep quick procedure with exertion for pulse f = 170 minus age (375–450)	To be repeated the following two days. Daily exertion (10 or 2x5 min) is to be continued (cardiopulmonal minimal training)	25–30	People with sound heart, capable of exercise	Secures good health a performance capacity Prevention and high
3 GK 2-II	15 min O ₂ multistep immunostimulation (375–450)	oral dose e.g. of thymus dragees (1x3+44 = 47 dragees)	25–30	People with sound heart, capable of exercise	General cancer prophylaxis, if repeated annually. Increased resistance to diseases
4 GK 2-III	25 min O ₂ multistep fever procedure (625)	(Therapeutic use of the increased COP and RMV occurring in high fever, mobile O ₂ MT ward)	25	Patients in the final stage of high fever	Reduction of rehabilitation time to just a few hours. Reduced risk
5 GK 2-IV	30 to 60 min O ₂ multistep obstetrics procedure (before and during the expulsion phase) (900–3600)	(Adaption of the mother's greatly increased RMV)	30–60	Also older pregnant women	Increased physical strength before and after parturition. O ₂ deficiency in children avoided
6 GK 3	9 h O ₂ multistep short procedure 3 sessions of 3 h (3270–3780)	Oral dosage of 2x20 mg Alupent® as in Fig. 140 3 HOT* treatments; one before each session	6–7	Physically disabled or otherwise weakened patients (coma-like states)	Emergencies Unconsciousness Paralyzed patients States after stroke
7 GK 4-I	36 h 18 day O ₂ multistep therapy procedure (8640)	Whenever possible, 2 min physical exercise at 20 min intervals during each session	4	Also immobile or disabled patients, older people, patients with cardiac insufficiency	Prevention of: O ₂ deficiency, illnesses, physical complaints. Improved quality of life and strength
8 GK 4-II	36 h 18 day O ₂ multistep therapy procedure and mini- mal training (to increase the COP) (8640)	RMV increase by sympathico- mimetic (e.g. Alupent®) optional after each of session, 10 min exercise without O ₂ application	4	Mobile people	Dangers of illnesses reduced Life expectancy increased

9 GK 4-III	Intensive variant of the 36 h 18 day O ₂ multistep therapy procedure (8640)	With 5 HOT* (UVB) treat- ments and optional measures as for GK 4-II	4	Also immobile or disabled patients	Circulatory disorders Nursing cases
10 GK 4-IV	36 h 18 day O ₂ multistep immunostimulation (8640)	With oral dosage of thymus dragees or (and) other immunomodulators (18x3+27 = 81 dragees)	4	Patients with low resistance, cancer patients in stage I after primary Ca-therapy	Reduced susceptibility to disease. Prophylaxis against cancer (Repeat once yearly)
11 GK 5	O ₂ multistep immediate aid procedure (≥ 1200)	To begin, one HOT* (UVB) treatment. 0.25 mg g-strophanthin i.v.	10	First aid in emergen- cies and in high fever	Amelioration of late effects of strokes, poisoning, burns
12 GK 6	O ₂ multistep long-term aid (3600 per day)	Strodival daily	25 virtually permanently	Critically reduced lung function	Elimination of pulmonally conditioned breathing difficulty. Improved quality of life
13 GK 7	Hyperbaric O ₂ multistep quick procedure with phy- sical strain (pulse f = 170 minus age) (450)	Optional: HOT* (UVB) or (and) hemodilution before treatment. Most intensive variant	30	Nursing cases	Severest circulatory disturbances
14 KA 1	80 min O ₂ multistep nicotinic acid procedure (480)	Nicotinic acid 0.5 g Vitamin C 0.5 g Procedure repeated after 7-14 days	6 during flush	People with sound heart	Hypotonia/regulatorily conditioned
15 KA 2	O ₂ multistep supplementary procedure after GK 2, GK 3 or GK 4 (600-1200)	Redistribution of blood volume into local target area. Regional hyperthermia	10-20	Severe cases requiring 2-step treatment	Severe local circulatory disorders

Table 24 Variant GK 1: O₂ multistep sauna cure procedure with lasting effect, exemplified by a treatment course with 18 saunas (e.g. 4 per week). Visit to the sauna: footbath 37 °C and 43 °C alternately. 1st sauna 10–20 min until core temperature $T_N \sim 39^\circ\text{C}$ – 15 min pause with alternately footbath. 2nd sauna as for the 1st, followed by full bath 18°C



¹ If desired, add 1 g vitamin C

² Measurement of the arterial and venous P_{O_2} , at rest and at the same time of day (no food, no coffee or tea etc. before), in blood samples taken from the "arterialized" ear lobe and from the unbound cubital vein, respectively, using a special instrument, e.g. Universal P_{O_2} meter, type MO 10, made by VE Kombinat Präcitronic, 8016 Dresden/DDR — or, alternatively, spirometric measurement of the O₂ uptake, at rest

³ Daily dose of Oxygenabund 30 min before exercise causes reduction of $P_{O_2\text{-ven}}$

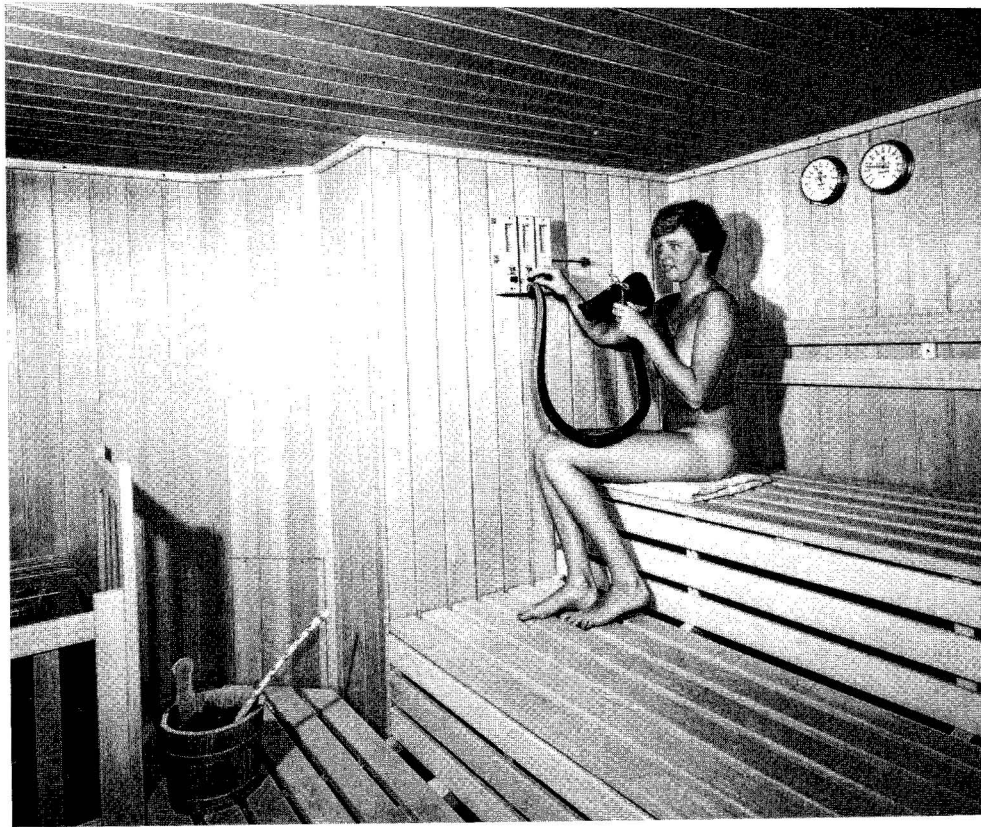


Fig. 218 Equipment for the O_2 MT sauna cure procedure (I). View of the sauna with the connection and dosing devices for the heat-resistant O_2 applicators. Klafs-Saunabau, Schwäbisch Hall, FRG

even often a rise in the PO_{2-art} with thermal strain, as the example in Fig. 220 proves.

The impressive increase shown in the PO_{2-art} with the O_2 MT sauna has two effects with great consequences for the use of the sauna in the health system:

1. **The reaching of a higher temperature and the duration of hyperthermia in the O_2 MT sauna.** It is generally assumed that the effects of a sauna are more pronounced the higher the body core temperature reached at the end of the sauna course is and the longer the period of hyperthermia lasts [330, 332]. Both components of the "sauna thermal dose" are increased greatly in the case of the O_2 MT sauna, as can be seen from the investigations in Figs. 221 and 222. These facts entitle us to expect the prophylactic and therapeutic effects of the O_2 MT sauna to be significantly superior to those of a normal sauna.

2. **The inclusion of patients for sauna treatment who, because of their conditions, cannot tolerate a normal sauna.** Even, and especially, in patients with already reduced PO_{2-art} or PO_{2-ven} reducing under exertion (and increased PO_{2-ven} , too), there are very great increases in the PO_{2-art} under O_2 MT conditions, as we have seen. It can be observed with the improvement in the circulatory condition thereby occurring, that even patients whose ability to tolerate the sauna was initially in doubt, can be admitted to the sauna procedure. This observation was confirmed by Krauss [84] in four borderline cases. One of these is shown in Fig. 223.

The special units shown in Figs 170 and 171, whose construction is adapted to the climatic conditions in the sauna, were developed for individual dosage of O_2 from pressure cylinders. Similar units are produced by Allihn (Munich, FRG).

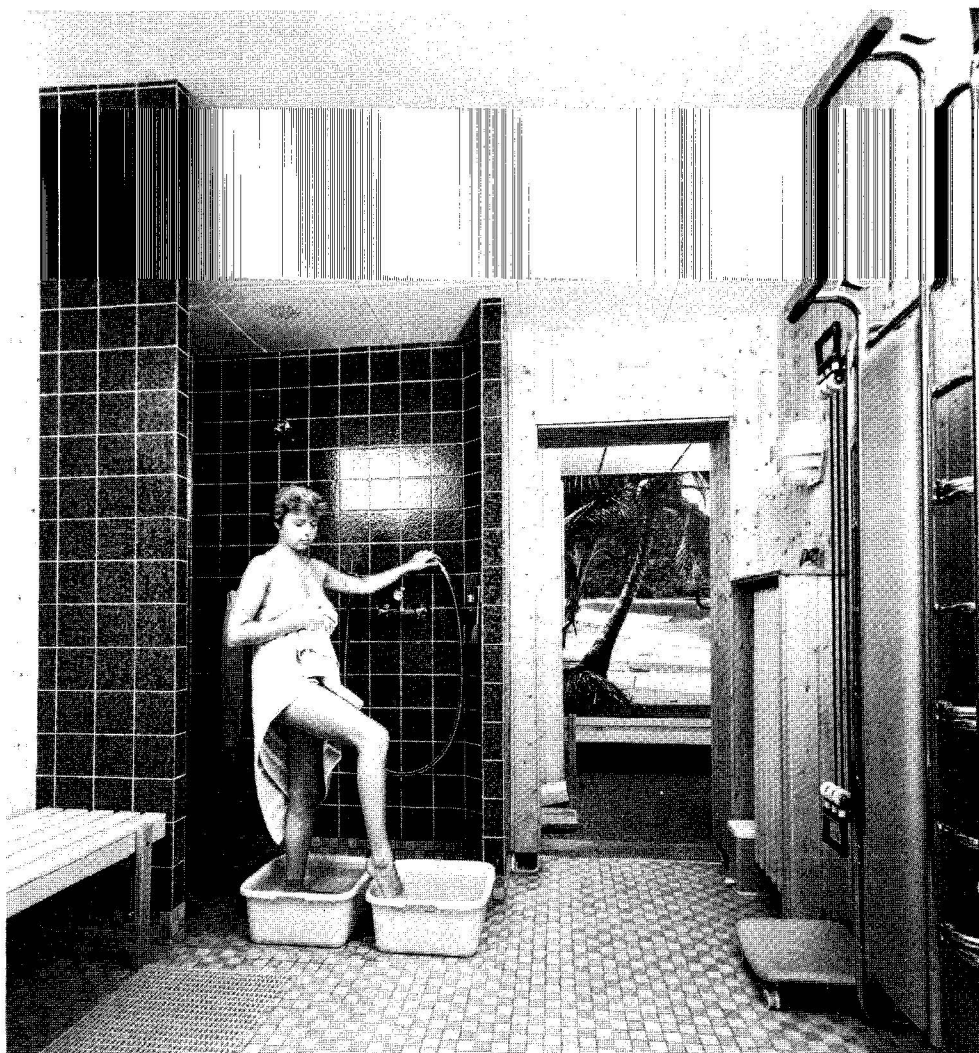


Fig. 219 Equipment for the O_2 MT sauna cure procedure (II). View of 18° and 43°C footbath tubs, shower and, right view of a solarium. Klafs-Saunabau, Schwäbisch Hall, FRG

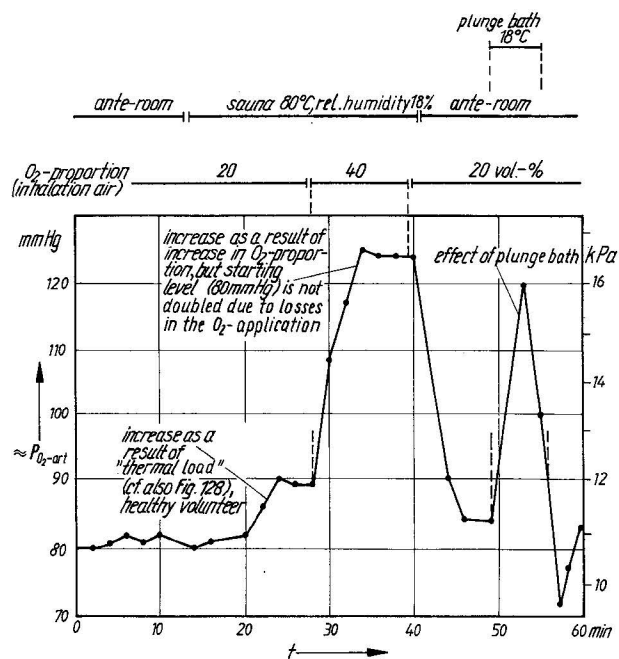


Fig. 220 Measurements of the arterial PO_2 to study the effects connected with a visit to the O_2 MT sauna

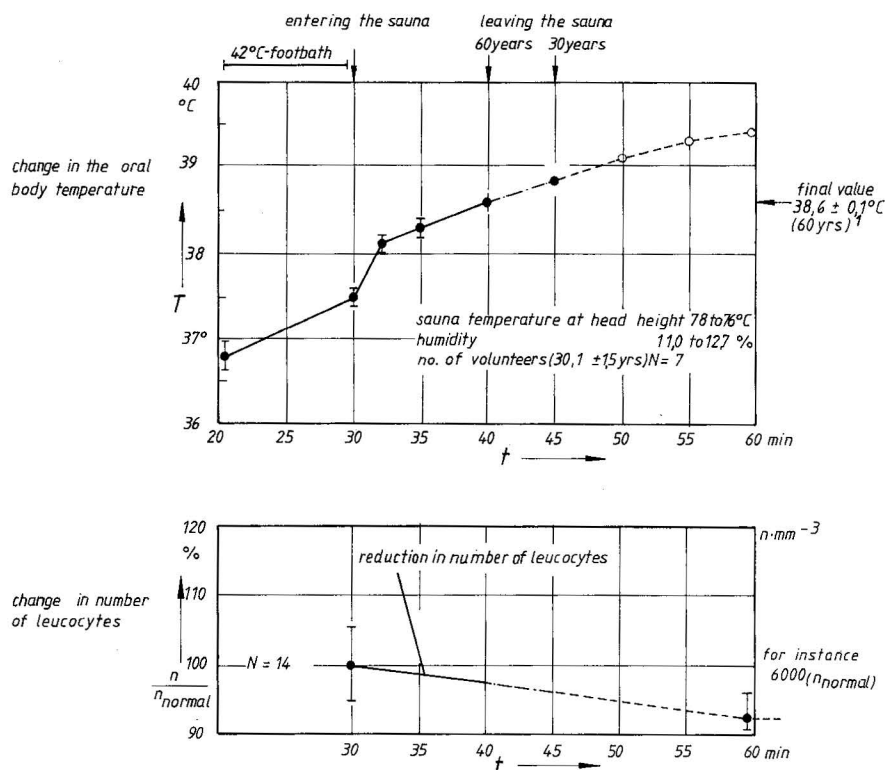


Fig. 221 Rise in oral body temperature T and change in number of leucocytes n as a function of the duration of the visit to a normal sauna according to [334]. Supply of 4 l normal air per min via applicator

¹ Age group 30 years: arterial resting P_{O_2} 96 ± 1.5 mmHg; pulse 110 ± 6 min⁻¹

The temporary increase in the O_2 metabolism of the tissue (increase in the CO_2 production, at rest) by approximately a factor of 1.7, which is to be expected in all O_2MT variants with (thermal or mechanical) exertion, is accompanied by considerable cardiovascular strain

during the procedure (see also the increase in pulse frequency in Fig. 223, right). For this reason there should be a *resting interval* of 10–20 min immediately after the end of the procedure in all therapy variants of this type.

4.2.2 15 min oxygen multistep therapy quick procedures, GK 2-I, GK 2-II, GK 2-III and GK 2-IV

Variant GK 2-I: The programming of this 15 min O_2MT quick procedure is summarized in Table 25. On the basis of measurements on many volunteers the O_2MT quick procedure [6, 337, 338] with the lasting increase in the $P_{\text{O}_2\text{-art}}$ and the reduction in the $P_{\text{O}_2\text{-ven}}$, accompanied by an increased O_2 uptake and CO_2 production (all values measured at rest), was developed from the simple O_2MT gymnastics [2, 9, 336].

Examples of *indications for the O_2MT quick procedure* are:

1. Compensation for a lifestyle with little physical activity
2. Combatting the effects of stressful influences
3. Stabilization of the circulation
4. Prophylaxis against O_2 deficiency and diseases of old age
5. The fast elimination of conditions of weakness
6. Application in fitness centers
7. Combatting sudden loss of hearing

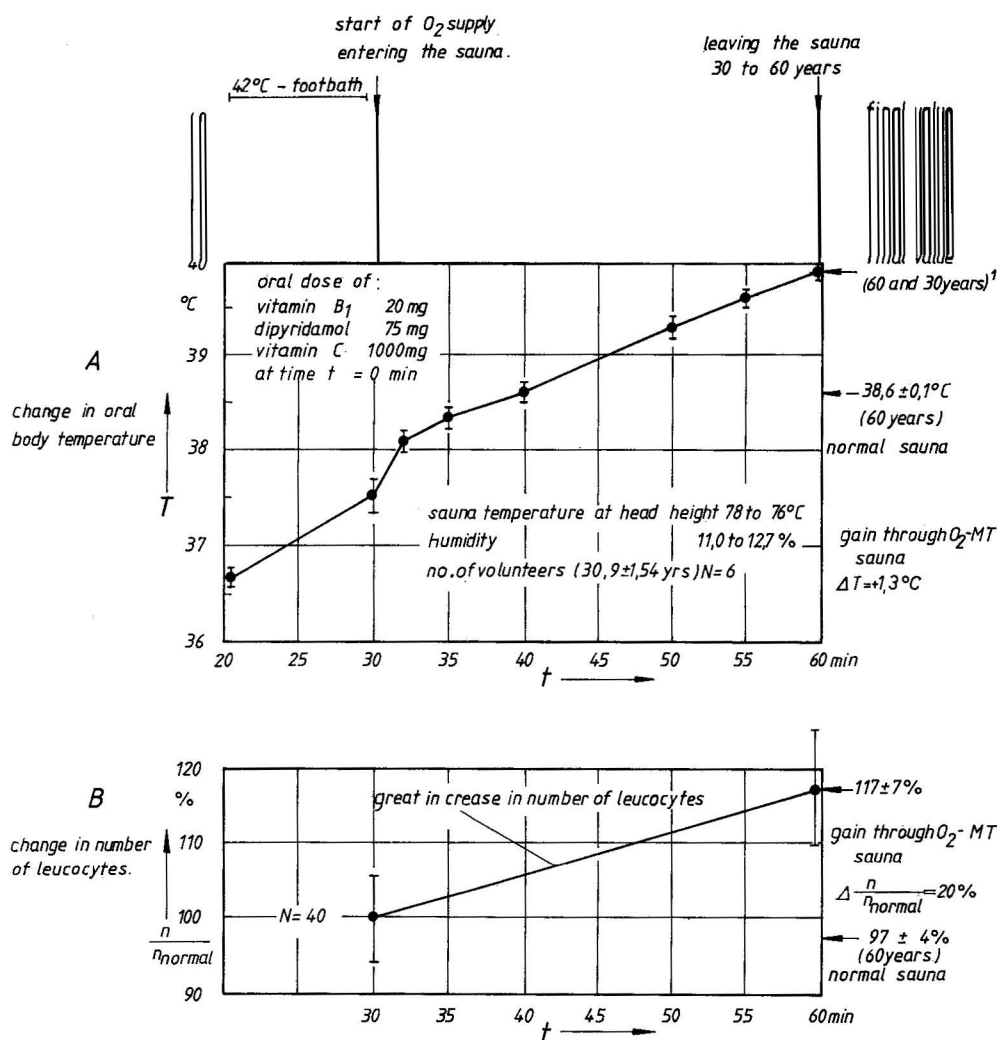


Fig. 222 Rise in oral body temperature T (A) and in the number of leucocytes n (B) as a function of the duration t of the visit to the O_2 MT sauna according to [334]. Supply of 4 l O_2 per min via applicator. Result: Instead of after $t = 10$ min as in the normal sauna (increasingly felt circulation stress), the O_2 MT sauna is not left until $t = 30$ min. As a result of this, even the age group of 60 years reaches an oral body temperature $T = 40^\circ C$. Simultaneously the number of leucocytes is 20% higher. A strong stimulation of the immunological defense system is caused by the O_2 MT sauna, preferably when combined with daily administration of immunomodulators, such as thymus preparations (e.g. Neythymun) over the period of the O_2 MT sauna cure

¹ Age group 30 years: arterial P_{O_2} during O_2 inhalation 127 ± 3 mmHg, pulse 115 ± 5 min⁻¹

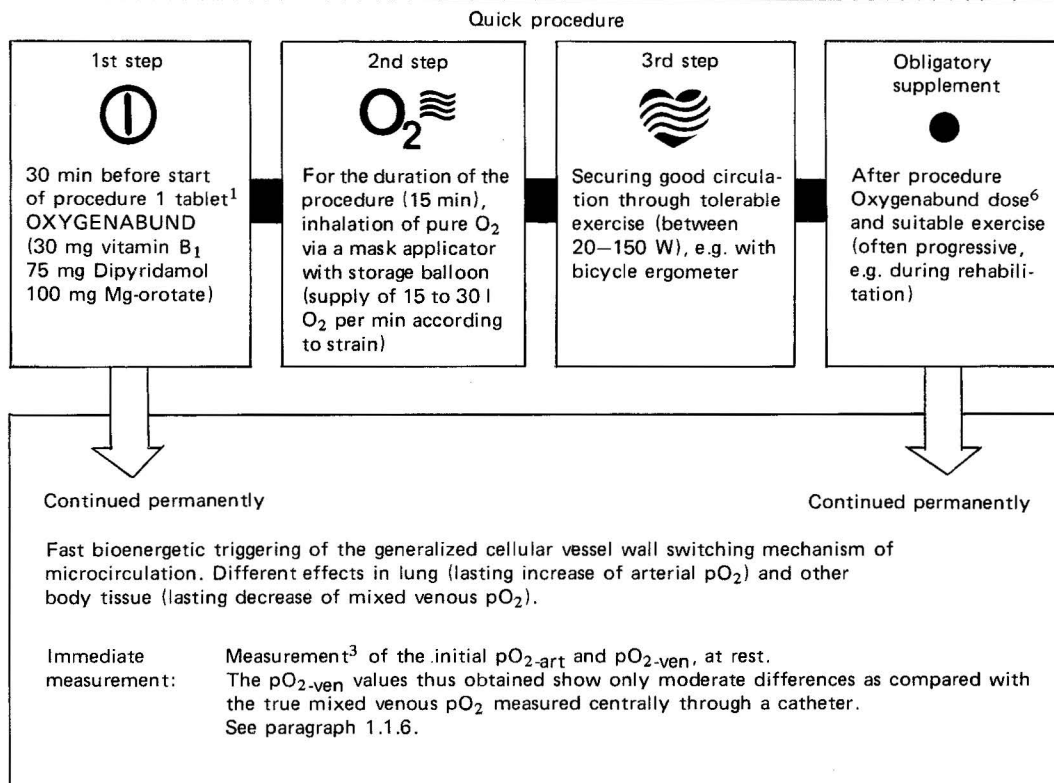
The quick procedure, like the short procedure discussed in the following section, is *contraindicated* for patients with manifest or pronounced hypertonia (stage III/IV, WHO), with signs of cardiac decompensation, with stenocardia syndrome at rest and, to some extent, with febrile infections.

The procedure must be prematurely interrupted, if any dangerous signs during physical exertion occur (WHO recommendation). In connection with this we would refer the reader to the example in Fig. 224 which shows from the course of the pulse rate how an older patient in need

of therapy could still be successfully treated with the 15 min O_2 MT quick procedure by gradually altering the physical exertion before and during O_2 application (conditioning). The increase in the physical performance capacity even during the O_2 MT procedure, which can also be seen from this figure, deserves great interest.

Many years ago, the former head of the 1st Medical Clinic of the Berlin Charité, our friend Theodor Brugsch, gave the author the following advice for the maintenance of good health in older age: "Be out of breath for 10 minutes each

Table 25 Variant GK 2-I: 15 min O₂ multistep quick procedure for sufficiently mobile individuals: Increased circulation through physical strain adapted to the individual case and a high O₂ supply via a mask applicator with storage balloon (cf. Fig. 150), corresponding to the RMV. Two repetitions, each after 2 to 7 days². If, in individual cases (phase of rehabilitation after illnesses, operations etc.), the physical activity cannot (or not yet) be carried out with the bicycle ergometer (e.g. home trainer, type Golf, made by Kettler, D-4763 Ense Parsit/FRG), simple step climbing (cf. Figs 151 and 153) or manual devices (crank handle ergometer made by Battert, D-4722 Ennigerloh/FRG; spring pressure gauge adjustable between 1 and 70 W, made by Maxi Power HB, S-500 02 Boras/Sweden) offer good alternatives



Cure success measurement:

Measurement approx. 2 days after end of therapy procedure.

Control measurements:

After months to years to establish whether a repetition of the procedure is necessary. Determination of O₂ status with η -nomogram.

¹ If desired, 1 g vitamin C

² Always after severe distress (phases of restricted mobility, illnesses etc.). Here, often one repetition is enough, or even one single treatment

³ Measurement of the arterial and venous P_{O_2} , at rest and the same time of day (no food, no coffee or tea etc. before), in blood samples taken from "arterialized" ear lobe and from the unbound cubital vein, respectively, using a special instrument, e.g. Universal P_{O_2} meter, type MO 10, made by VE Kombinat Präcitronic, 8016 Dresden/DDR

⁴ Strain such that pulse = $f \sim 170$ minus age

⁵ Strain is slowly increased from 5 min before start of procedure (starting phase)

⁶ Daily dose of Oxygenabund 30 min before exercise causes drop of the P_{O_2-ven}

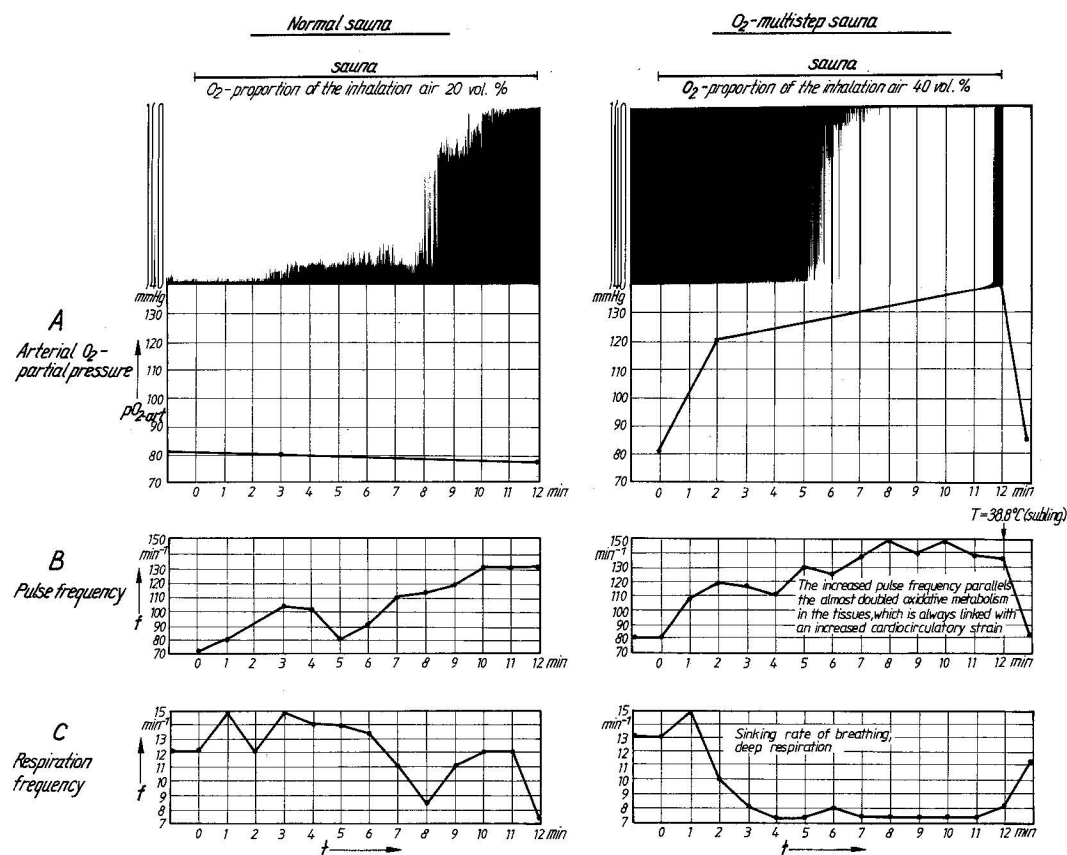


Fig. 223 Behavior of arterial P_{O_2} , pulse frequency and respiration frequency in a patient suffering from severe bronchial asthma with spirometric and roentgenological signs of lung emphysema and pulmonary heart disease with beginning decompensation, after visits to a normal and the O₂MT sauna: the latter is tolerated extraordinarily well (according to Krauss [84])

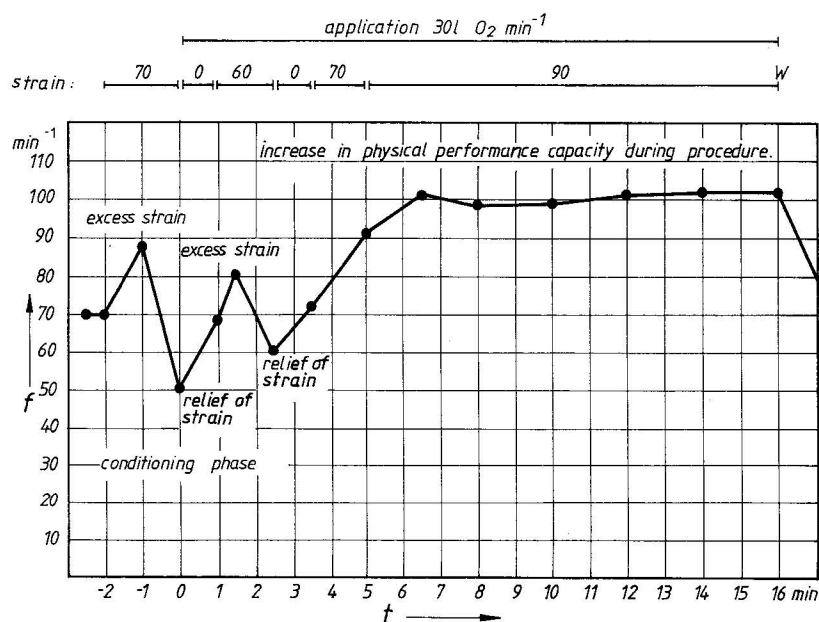


Fig. 224 Pulse frequency (f) (as an indicator), conditioning and increase in physical performance capacity during the 15 min O₂MT quick procedure in a 73-year-old patient in need of therapy

day!" The deeper meaning of this recommendation was that once a day an increase in the O_2 metabolism of the cells and tissue and a periodic increase in the strain on heart and lungs were to be brought about. The 15 min O_2 MT quick procedure and the daily minimal training demanded afterwards, as in Fig. 153, fulfil Brugsch's recommendation. This procedure, already discussed in detail in Paragraph 1.1, and especially in 1.1.9.4, is the variant of the O_2 MT which leads to the greatest increase in the O_2 metabolism in the endothelial cells of the terminal capillary bed, and as a result of physical exertion (increase in COP and RMV, highest O_2 flow taken up by lungs, highest PO_{2-art} during O_2 application, increased blood flow in capillaries). This means that this variant, with a duration of only 15 min, is sufficient for the "high-charging" of the blood microcirculation or of the O_2 uptake at rest.

The 15 min O_2 MT quick procedure is a variant with weighty prophylactic indications, intended mainly for those who are still healthy or for those with functional disorders, and it should have a wide field of application in cure institutions (fitness centers). In healthy persons the increase in circulation occurring during physical exertion is accompanied, as the measurements in Fig. 225 show, even without additional O_2

application by an increase in the PO_{2-art} . With O_2 application at a flow rate of 30 l/min PO_{2-art} levels of up to 350 mmHg (23.5 kPa) were measured, as documented in Fig. 3.

After decades of regular sport in youth and middle age, the O_2 MT should not be begun too late. Many of the pathological phenomena, which are caused primarily by O_2 deficiency or reduction in the resting PO_{2-art} and O_2 uptake, and which develop slowly in the course of many years, and which, after all, can determine the fate of the individual, are of *reversible character in their early phase*. The chance to set a favorable course by deciding to undergo prophylactic treatment before the symptoms of the disease become manifest therefore only exists for a limited period of time. Here, too, the individual can do a great deal in addition to therapy. The levels of the arterial and venous PO_2 , measured at rest, and the η -value derived from these, are high-ranking relative characteristic values for the O_2 situation, or the acute energetic situation. These values not only depend on age and therapy, but also on body mass. Figure 226 gives quantitative information on this. According to this figure, for example, the same reduced PO_{2-art} in a slim 20-year-old is to be expected as in a heavily overweight 45-year-old. Parallel to the use of the O_2 MT,

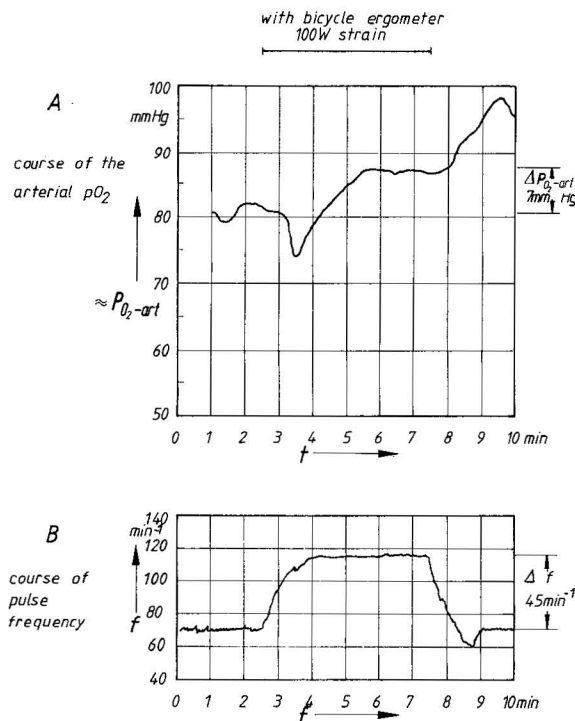


Fig. 225 Transcutaneous registration of the arterial PO_2 and the pulse frequency of a healthy 39-year-old man, breathing air, during physical strain of 100 watt for 5 min [255]

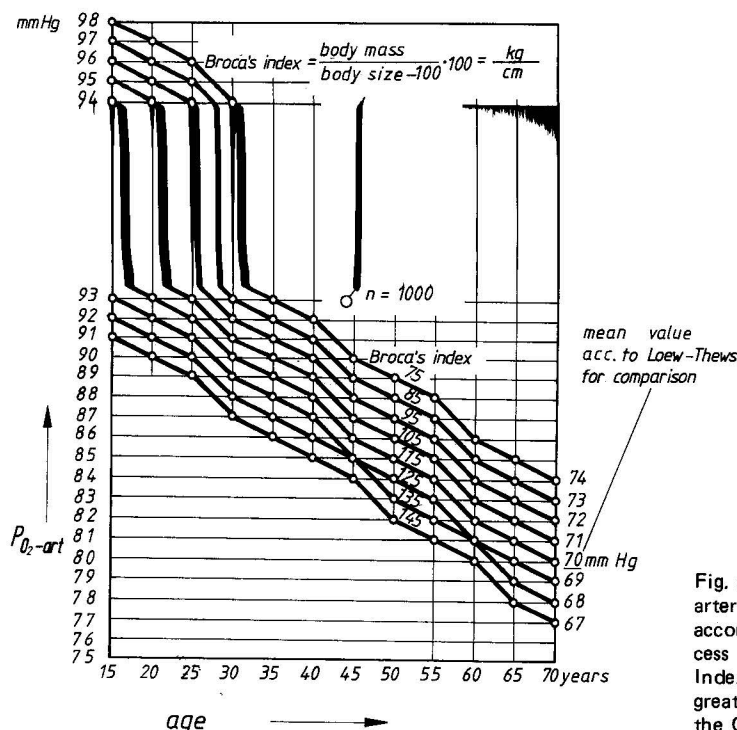


Fig. 226 The dependence of the arterial P_{O_2} on age and body weight according to [339]. The loss of excess weight (reduction of the Broca's Index) should be strived for with great perseverance and willpower when the O_2 MT is used

the patient must therefore strive, with great willpower and perseverance, to eliminate excess weight using proven methods (e.g. regular exercise, clinically implemented fasting).

Variant GK 2-II: The addition of the further step of immunomodulation [340] produces the important variant shortly termed *15 min oxygen multistep immunostimulation* (O_2 MI). Among the numerous effective immunomodulators known today (2-cyanoethyl urea [341, 342], PIND-AVI [343], Neytumorin [344], Bestatin [345]), the thymus preparations [340, 346] in particular have been increasingly used in the last few years.

We anticipate the following in terms of the effect of this variant: it could be estimated in the in vivo application of O_2 MI against cancer that, expressed by the number of destructible cancer cells, there is progress by several powers of ten compared with the defense potential in a normal middle-aged person. The extent of the effect seems to stretch into the domain of therapeutic attempts, as in singular cases the disappearance of cancer foci of up to 10^9 malignant cells was observed.

The possibility of applying such procedures in the health service depends entirely on how far they can be simplified. This applies to both the O_2 MT procedure and the type of application of the immunomodulator. In order to make possible a broader utilization, we are therefore working to combine in future the 15 min O_2 MT quick procedure, in particular (which requires little effort and can be easily implemented on

an outpatient basis), with oral application of the immunomodulating substance.

The condition for the good effect of this combination is that no loss of effect occurs when the i.v. or i.m. injection is replaced by the oral administration of the drug. Over a course of years numerous test methods to determine effect were studied in the Biochemical Section (head: Dr. W. Krüger) of our Institute. The leucopoiesis test (leucocyte/lymphocyte counts in peripheral blood) was found to be generally well reproducible and to contain sufficiently representative information, and was therefore used as the basis for most of the above quoted papers from our Institute. One of the advantages of this test is that it accords with the known clinical experience as to the increasing weakness of defense correlating with leucopenia. For this reason the comparison of the effect of oral administration and the i.m. injection of thymus preparations from the same manufacturer was carried out in [347].

The results obtained as to the rise in the number of leucocytes in the circulating blood after stimulation of the defense system by a single oral dose or i.m. injection of thymus preparations are shown in Fig. 227. The dosages necessary and used for the experiment with rats are also included in the figure, as are also the measured points for the control and for our standard reference substance, 2-cyanoethyl urea. The comparison shows that at least the same leucopoietic effect is obtained with the oral administration of the thymus extract from the Thym-

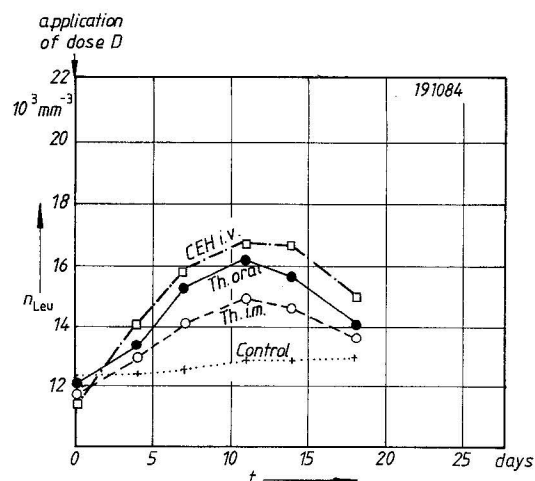


Fig. 227 Rise in the numbers of leucocytes n_{Leu} in the circulating blood following stimulation of the defense system by a single application of the following thymus extract doses: oral: $1/50$ dragee $200 \text{ g}^{-1} = 24 \text{ mg} \cdot \text{kg}^{-1}$; i.m.: $1/10$ ampoule $200 \text{ g}^{-1} = 3.25 \text{ mg} \cdot \text{kg}^{-1}$; result: oral dose and i.m. injection roughly reveal equal effectiveness. 45 Wistar rats δ , body mass 180 g. Thymus extract: Dr. K. Mulli KG, D-7844 Neuenburg, FRG. Oral dose: active substance from Thymus-Mulli dragees; i.m. injection: ISTP ampoules

Uvocal dragees as with i.m. injection of the thymus preparation ISTP.

If a temporary immunostimulation is sufficient, and if the main object is to obtain a particularly

strong effect, e.g. for general cancer prophylaxis or for the prophylaxis of cancer metastases, then three thymus dragees are administered 14 days before the start of the 15 min O_2MT quick procedure, with which they are combined, so that a strong stimulation of the new formation of defense cells is already effective during the procedure.

The programming of the 15 min $\text{O}_2\text{MI GK 2-II}$ is the product of the programming of the 15 min O_2MT quick procedure, GK 2-I, with the additional daily oral administration of thymus extract dragees. Figure 228 shows this programming in a simplified presentation. In particularly severe cases we add to the thymus dragees the strong and synergetically working PIND-AVI preparation and, if necessary, also selective overacidification of the cancer tissue [2, 140, 190] and even with slight hyperthermia up to 38.5°C by means of glucose catabolism, supported by the infrared A irradiation unit (Fig. 292).

The main indications for the GK 2-II variant are:

1. General cancer prophylaxis when repeated regularly at intervals of approximately one year,
2. Prevention of illnesses, strengthening of lowered resistance,
3. All indications of the GK 2-I variant.

The extension of the range of indications by the inclusion of the immunostimulation step is so significant that, considering the minimal

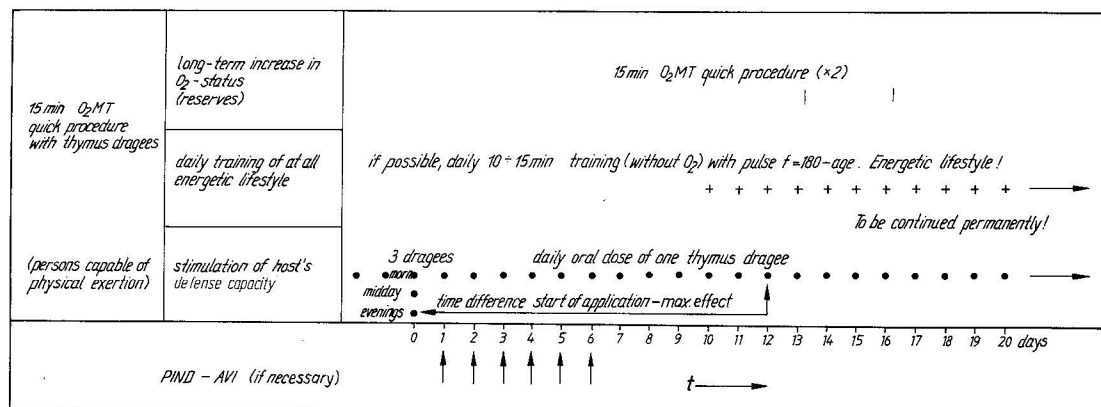


Fig. 228 The 15 min O_2MT immunostimulation variant GK 2-II. Continuation of the medication with thymus dragees (e.g. Thym-Uvocal, Dr. K. Mulli, D-7844 Neuenburg, FRG), one dragee daily over a further 30 days.

In special cases the immunomodulator PIND-AVI (Inst. of Medical Microbiology, Infectious and Epidemic Diseases, University of Munich/FRG) can also be applied, e.g. as follows:

2 mg (1 vial) i.m. per day on days 1-6 (synergetic effect through different effector mechanisms). In addition, the blood glucose level can be increased to $5 \cdot 10^{-3} \text{ g/ml}$ for 6-8 hours after both treatments in order to strengthen the chemotactic attraction of leucocytes to the foci (see text)

Variant GK 2-IV: The concept of the 120–60 min O_2 MT obstetrics procedure [18, 348] is methodologically closely related to that of the 25 min O_2 MT fever procedure. A naturally existing great increase in COP and RMV is again used to increase the O_2 status, and thus also the physical performance capacity, by means of the triggering of the switching mechanism of the blood microcirculation during and after the procedure.

It hardly needs to be pointed out that the *birth process*, from the beginning of the labor pains right up to almost the end, exhausts the woman's strength and energy reserves. This applies even more to women over 35 or with existing diseases, in whom the energetic status has already sunk noticeably compared to the status in youth. During the expulsion phase (RMV up to 60 l/min) critical energy, i.e. oxygen, deficient conditions can therefore often arise in the child, which is still supplied from the mother. It is known that this deficiency can cause damage of a considerable proportion of

the child's brain cells. The measures summarized in Fig. 229 should be applied in order to prevent these deficiency phenomena which can have drastic effects on the child. In the mother there occurs a significant increase in the physical performance capacity in the expulsion phase (150–200 watts) due to the increased production of chemical energy (energy-rich phosphates, process of birth shortened). In addition to this there is a lasting improvement in the O_2 status of her organism after birth, caused by the triggering of the switching mechanism of the blood microcirculation (the resting value of η is roughly doubled). Pilot treatments were so favorable that they have been continued. During administration of 50 l O_2 /min no critical increases in cord blood PO_2 were observed. The brightness of the mothers after birth was particularly striking. If the measures given in Fig. 229, left, are also applied (combatting of placenta insufficiency by previous O_2 MT treatment), there should be a better situation for women between 35 and 45 in this question in future.

4.2.3 9 h oxygen multistep therapy short procedure GK 3 and GK 3-I

The *program of the 9 h O_2 MT short procedure, GK 3*, is presented in Table 26. In this short procedure the O_2 application occurs via a mask applicator with storage balloon and of a flow of 6 l O_2 /min. The increase in the COP and the correlating RMV is brought about in these short procedures by stimulating drugs, e.g. sympathicomimetics such as Mesocarb, Dopamin analogues, Alupent (cf. Table 14 and Fig. 140). This variant is therefore mainly intended for the large number of patients who are not, or not sufficiently, able-bodied or who, for various reasons, cannot undertake or tolerate physical exertion.

The *main indications for the O_2 MT short procedure* are, e.g.:

1. Bringing the patient out of general debility or unconsciousness
2. Speeding up of rehabilitation
3. Stabilization of the circulation in motor-paralyzed patients
4. Stabilization of the circulation in immobile patients
5. Stabilization of the circulation in physically disabled patients
6. Building-up of energetic reserves before foreseeable stress
7. Elimination of side-effects of "doping" drugs

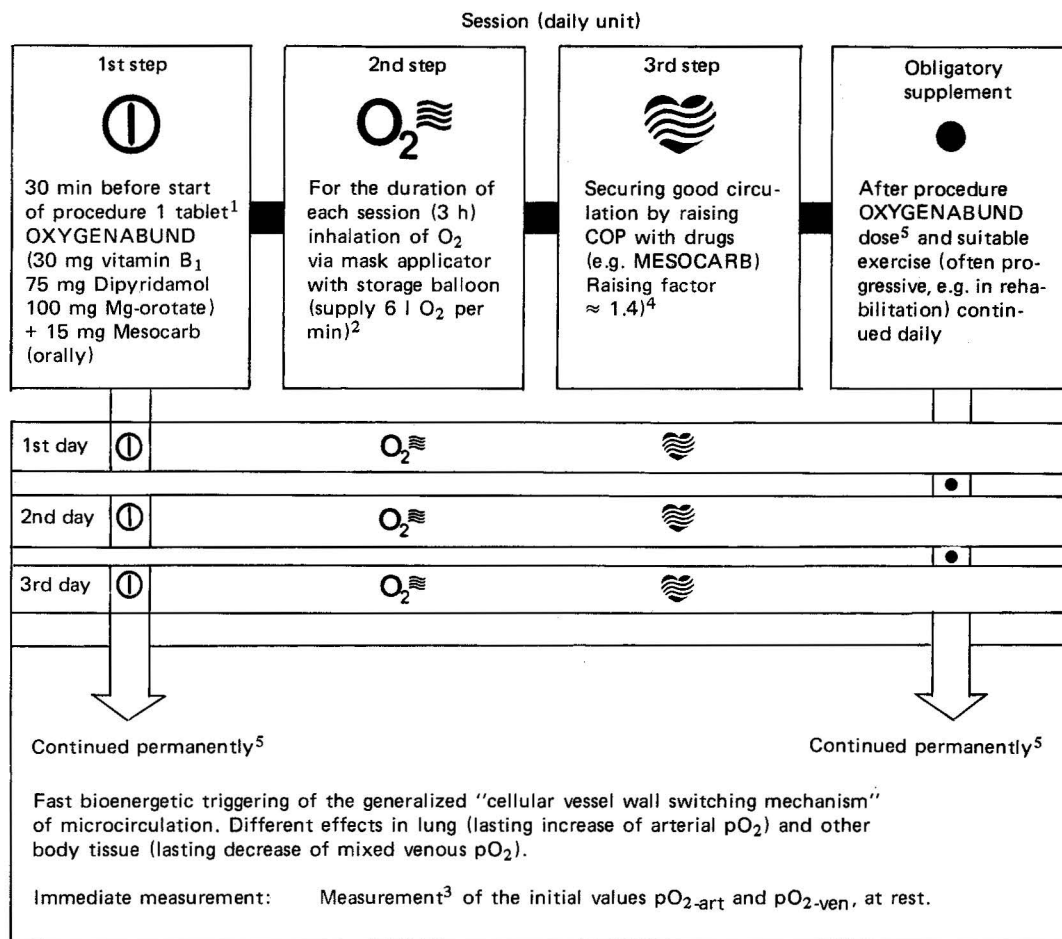
8. Aid in resuscitation from coma lasting several days
9. Immediately after stroke, to reduce deficiency symptoms

Contraindications have already been discussed in Paragraph 2.3.3.

Variant GK 3-I: 5 x 20 min O_2 MT short procedure with lasting effect for sufficiently mobile patients with adequate stress capacity but with little time. See Appendix for programming. The RMV is increased to 12 l/min by means of moderate physical exertion during five 20 min sessions taking place within say 5 days (roughly 40 watts, supported, if necessary, by administration of one 20 mg Alupent per session). The O_2 flow is adjusted to also 12 l/min, using a mask applicator with storage balloon.

In terms of effect (PO_{2-art} , PO_{2-ven} , η , O_2 uptake) and time required, this variant lies between the 15 min O_2 MT quick procedure discussed in the last paragraph and the 36 h O_2 MT (standard) procedure dealt with in the next. In patients who would normally be given the 36 h variant but cannot spare the 18 (or 9) days for it, and still have a moderate stress capacity, the increase in circulation necessary for the short procedure can also be brought about by slight physical stress. This is a fruitful field for further

Table 26 Variant GK 3: 9 h O₂ multistep cure procedure with lasting effect for disabled patients being incapable of strain. Improvement of circulation by drugs. In special cases supplementation by HOT* (UVB) treatment and additionally for individuals having little time, by weak physical exertion (25–50 W) during the 3 h sessions



Cure success measurement:

Measurement approx. 2 days after end of therapy procedure.

Control measurements:

After months to years to establish whether a repetition of the procedure is necessary. Determination of O₂ status with η -nomogram.

¹ If desired, add 1 g vitamin C

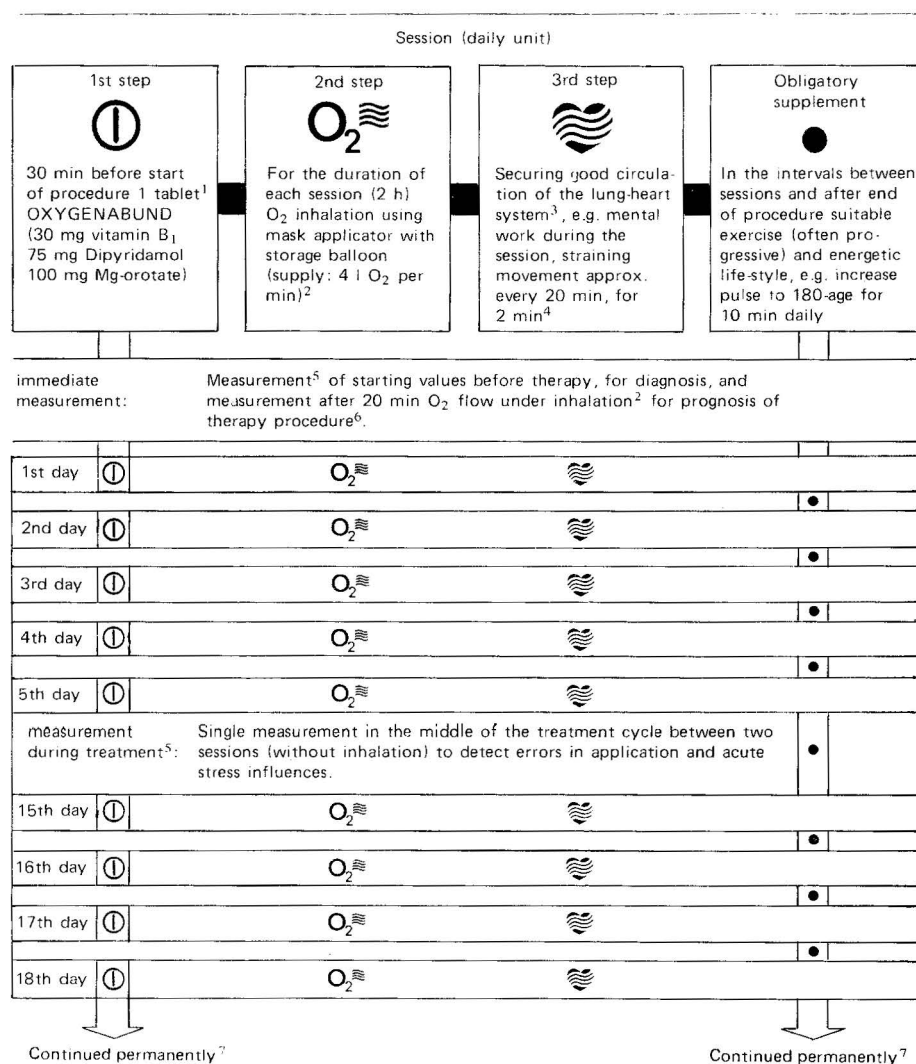
² Check O₂ flow and fit of mask applicator

³ Measurement of the arterial and venous P_{O₂}, at rest and at the same time of day, in blood samples taken from the "arterialized" ear lobe and from the unbound cubital vein, respectively, using a special instrument, e.g., Universal P_{O₂} meter, type MO 10, made by VE Kombinat Präcitronic, 8016 Dresden/DDR

⁴ Equivalent to approx. 30 W strain. See also Fig. 140

⁵ Daily dose of Oxyge nabund 30 min before exercise causes drop of P_{O_{2-ven}}

Table 27 Variant GK 4-I: 36 h/18 day O₂ multistep therapy procedure with lasting effect. Standard variant "18-day cure" (as on 31.12.1986). Further variants: 9 sessions of 4 hours ("9-day cure") or 5 sleeping cures of 7 hours ("5-night cure"). In special cases completion by HOT* ("Intensive variant" GK 4-III)



Cure success measurement⁵:

Measurement approx. 2 days after end of therapy procedure.

Control measurements⁵:

After months to years to establish whether a repetition of the procedure is necessary. Determination of O₂ status with η -nomogram.

¹ If desired, add 1 g v itamin C

² Check O₂ flow

³ For hypotensives: increase blood pressure amplitude by drugs (e.g. Novadral Retard or Mephentermin)

⁴ Not for sleeping cure

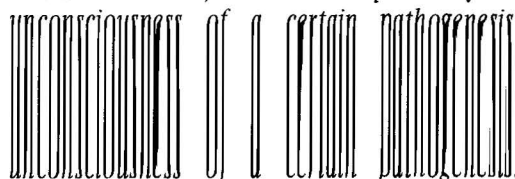
⁵ Measurement of the arterial oxygen partial pressure (P_{O_2-art}) in capillary blood taken from the "arterialized" ear lobe after 10 min rest at the same time of day (no food, no coffee or tea etc. before), using a special instrument, e.g., Universal P_{O_2} meter, type MO 10, made by VE Kombinat Präcitrönic, 8016 Dresden/DDR

⁶ $P_{O_2-art} > 125$ mmHg indicates good response

⁷ Daily dose of Oxygenabund 30 min before exercise causes drop of P_{O_2-ven}

⁸ Drop in P_{O_2-art} particularly after strong stress influences like, for example, physical inactivity over several weeks, operation or infections

research. Experiments with this method (if necessary, supplemented by the O_2 activation method or HOT*) to resuscitate patients from



lasting several days, would also be interesting (colloquium with H. Gerstenbrand, University of Innsbruck, Austria, on 11.11.82).

4.2.4 36 h (18 day) oxygen multistep therapy procedure, GK 4-I, GK 4-II, GK 4-III and GK 4-IV

Variant GK 4-I: The program of the 36 h (18 day) O_2MT procedure, GK 4-I, is given in Table 27. It is the procedure [2, 3, 6, 20, 92, 159, 337, 338] with which the lasting restoration of the PO_{2-art} , at rest, which had sunk greatly in older age, was surprisingly discovered in 1977 [3] and in 1982 the similarly lasting reduction in the resting PO_{2-ven} [338]. It is also the variant which has so far been most frequently used on patients (sort of standard treatment) and which has been the most thoroughly studied (see Paragraph 1.1.8.4 ff). The sensible total duration of the procedure was set at 36 h because the PO_{2-art} level (cf. Fig. 39) and the PO_{2-ven} level did not improve with a greater number of hours. When well organized (2 min exercise every 20 min, mask applicator etc.), the time required for this variant can be reduced to 30 h of treatment within 15 days. It enables the patient to adapt better to the normal 3-week cure course. This rather time-consuming variant has the advantage that a particularly strong increase in the resting PO_{2-art} is observed with it (strong lung regeneration), and that it can also be used for patients with little stress capacity and who are disabled. Three types of timing of the procedure are preferred at present: a 9-day cure with 9 sessions of 4 h (out-patients and in-patients), the 18-day cure with 18 sessions of 2 h (usually for outpatients) and the 5-night cure with 5 treatments of 7 h during sleep (in-patients).

Indications for the 36 h O_2MT procedure are:

1. Regeneration of the lung-heart system, universal prophylaxis
2. Support for the drug treatment of heart and circulation
3. Oxygen deficiency diseases
4. Diseases and complaints of old age, senile diabetes
5. Angina pectoris, cardiac arrhythmias
6. Retinopathies, loss of visual field, light sensitivity
7. Sudden reduction of visual acuity, cataract
8. Not yet established hypertension (stages I and II WHO)
9. Arteriosclerosis, coronary sclerosis
10. Peripheral circulatory disorders
11. Disorders of the energy balance of the brain, defective memory, migraine, sleep disorders

12. Liver, especially when damaged by alcohol, cirrhosis of the liver
13. Disorders of the kidney function
14. Chronic bronchitis
15. Lung emphysema
16. Speeding-up of rehabilitation, wound healing
17. Alleviation of toxic stress and the side-effects of aggressive drugs
18. Increased physical and mental performance capacity, and quality of life
19. Combat of placenta insufficiency

The 3rd step of the program will be chosen very differently according to the stress capacity of the cure participant. Good circulatory condition is often sufficient in this long-term variant to reach the desired increase in the η -value. If the patient is able to tolerate it, coffee should be drunk in order to increase the PO_{2-art} and the COP slightly. The supplementation of the program by exercise training in the intervals between the treatment sessions is obligatory, except for disabled patients; see 2.3.7 for the type of exercise training. For non-able-bodied patients, a low dose of Alupent is given before each session.

In special cases, e.g. in patients with a very low pretherapy level of the PO_{2-art} , in whom it is important to achieve an additional intensification of the regeneration, it is recommended that the O_2MT procedure be performed in the variation with 6 sessions of 2 h per week over 21 days, and that it be supplemented by a dose of 14 mg *Buphenin hydrochloride retard*, i.e. one capsule Penitardon three times daily (e.g. at 7.00, 15.00 and 23.00 hours). This recommendation is based on an experiment with similar medication and similar timing on 10 patients with a mean PO_{2-art} of hardly 50 mmHg (angio-organopathies of the most varied location, in stages III and IV according to Fontaine), whose PO_{2-art} rose to 80 mmHg with this medication [349].

In cases of increased resistance to therapy in chain smokers with up to 15% CO poisoning of the hemoglobin, it can be necessary to perform an Hb detoxification [18] before the procedure and even to raise the total number of treatment

hours to up to 60. Conversely, it is often possible to reduce the duration of treatment, e.g. to 18–24 h, in patients in whom the O₂MT procedure must be repeated due to stress.

The tremendous speed with which the 36 h O₂MT procedure has been absorbed into healing practice allows us to conclude that the O₂MT should soon become a *universal methodological element of the cure system*. Its prophylactic effect is unusually broad because this procedure, as stated in the introduction, attacks the primary causes of many complaints and diseases.

With the developed zeolite devices whose performance is adapted to the high demand of the main variants of the O₂MT, equipment has arisen which, powered from the mains, provides inhalation air with increased O₂ content by means of oxygen enrichment of the atmospheric air (see Paragraph 3.2.4). Thus the time is approaching when air mixtures with a high O₂ content will be easily available even in the home. In the near future, therefore, the technical requirements will be met that will allow patients in need of O₂ to be able to apply variants of the O₂MT, of a gentle nature, in their private sphere under medical advice. One of the most important of these variants is the *O₂MT sleep*.

The idea of using the apparently unproductive sleeping time of a human prophylactically and therapeutically in an intensive way is fascinating. It is really true, for example, that a person in old age can in this way increase his O₂ status far above the best levels of his youth for 6–8 h of the 24 h cycle. It is also an enticing feature of this variant that it consumes no active time. A press of a button on the device switch before falling asleep is all that is required, and then the time spent asleep is used multivalently in the interests of health. An in-built switching-off system in the device ensures that, after a selectable period of time, e.g. 7 h, the current is automatically switched off, and the remaining sleeping time is spent normally.

In order to smooth the path towards the broad utilization of this variant, a technical task had to be performed: the *nonintrusive application of the O₂-air mixture*. The only technical solution that was admissible was one that would not be felt to be disruptive when falling asleep and that would not disturb sleeping habits. We believe that the mask applicator of soft synthetic material (with storage balloon), shown in Fig. 166, is a very good solution to this problem. A soft pillow is all that is needed to prevent the synthetic tube of the applicator

from being a nuisance when the patient lies on his side.

The 5-night sleeping cure is mainly suitable for persons under great stress (State officials, industrial managers etc.), who spend too little time on maintaining their health, yet are under extreme stress over a period of years. When their cure is suitably organized they can work at full capacity during the day and, due to the nightly 7 h treatment time, this variant consumes no productive time.

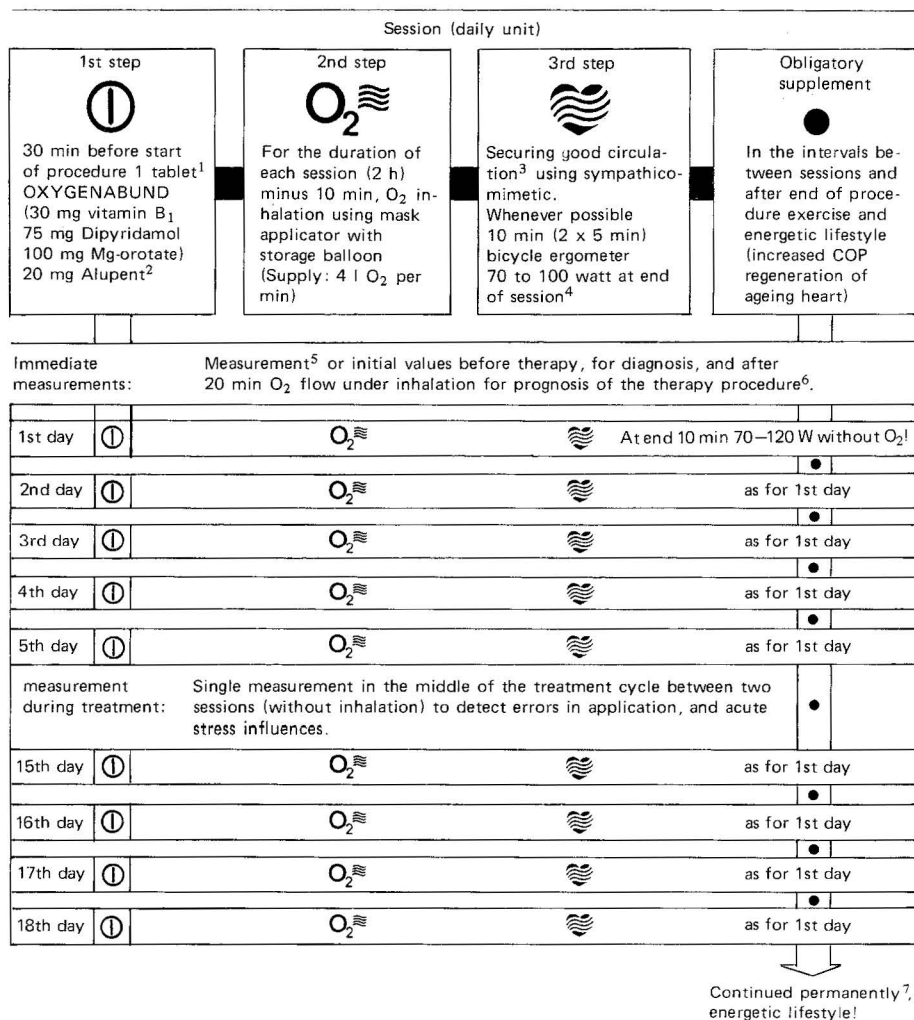
Variant GK 4-II: After the addition of measures to increase lastingly the COP by means of daily minimal heart training during the 18-day cure, there results a variant with the term *36 h (18 day) O₂MT procedure and minimal training* [37]. The concept of this variant is based on the result, presented in Figs 66–68, that the critical deterioration in the O₂ status with advancing age is due almost entirely to the drop in COP. It can be seen from sports medicine and, especially from the papers by Hollmann and his team in Cologne (FRG), to what extent and in what way the drop in COP can be alleviated by stamina training and sport in old age [269, 270]. A *cardiopulmonal minimal training* could be derived from these papers, which could be included in the 36 h (18 day) cure without any increase in the amount of treatment time required.

The program of the 36 h (18 day) O₂MT procedure and minimal training (GK 4-II) can be seen from Table 28. The decision whether to include the dose of Alupent (optional) rests with the doctor in charge. The minimal training of ten or 2x5 minutes duration, inserted at the end of the 2 h session, as in Fig. 230, takes place without O₂ application and aims at an increase in the pulse rate of $f = 180 - \text{age}$ (Hollmann's rule), characteristic for the aerobic/anaerobic threshold [270]. The inclusion of the minimal training in the framework of the 2 h session has the advantages of being easy to control and of eliminating additional time required. If these two aspects are unimportant, the minimal training, because it occurs without O₂ application, can also be undertaken somewhere else and at any convenient time, in accordance with the guidelines in Fig. 153. Such a process has the advantage that the patient becomes accustomed to such training in his own environment and is then more likely to continue the same minimal training daily for the "energetic lifestyle" demanded.

The main indications of the GK 4-II variant are:

Table 28 Variant GK 4-II: 36 h 18 day O₂ multistep therapy procedure and minimal training to raise the COP. With an additional contribution (according to condition and age) to functional heart regeneration by means of 10 min cardiopulmonal minimal training without O₂ inhalation at the end of each session, with pulse acceleration to the aerobic-anaerobic border. (Pulse frequency e.g. 110 in the 8th decade of life, and 130 min⁻¹ in the

6th. In special cases completion by HOT* ("intensive variant")



Cure success measurement:

Measurement approx. 2 days after end of therapy procedure.

Control measurements:

After months to years to establish whether a repetition of the procedure is necessary. Determination of O₂ status with η -nomogram⁸.

¹ If desired, add 1 g vitamin C

² Orziprenalin (Alupent®) 20 mg perlingual. For patients in poor condition, no dose until after 2nd or 3rd session (optional). Take contraindications seriously

³ Whenever possible, the COP to be determined at rest before and after the procedure

⁴ Due to effect of Alupent, these figures are 30 W lower than otherwise necessary for given pulse increase

⁵ Measurement of the arterial and venous peripheral P_{O_2} , at rest and at the same time of day, in blood samples taken from the "arterialized" ear lobe and from the unbound cubital vein, respectively, using a special instrument, e.g., Universal P_{O_2} meter, type MO 10, made by VE Kombinat Präcitronic, 8016 Dresden/DDR

⁶ $P_{O_{2-art}} > 125$ mmHg indicates good response

⁷ Daily dose of Oxygenabund 30 min before exercise causes drop of $P_{O_{2-ven}}$

⁸ Drop in $P_{O_{2-art}}$ particularly after strong stress influences like, for example, physical inactivity over several weeks, operation or infections

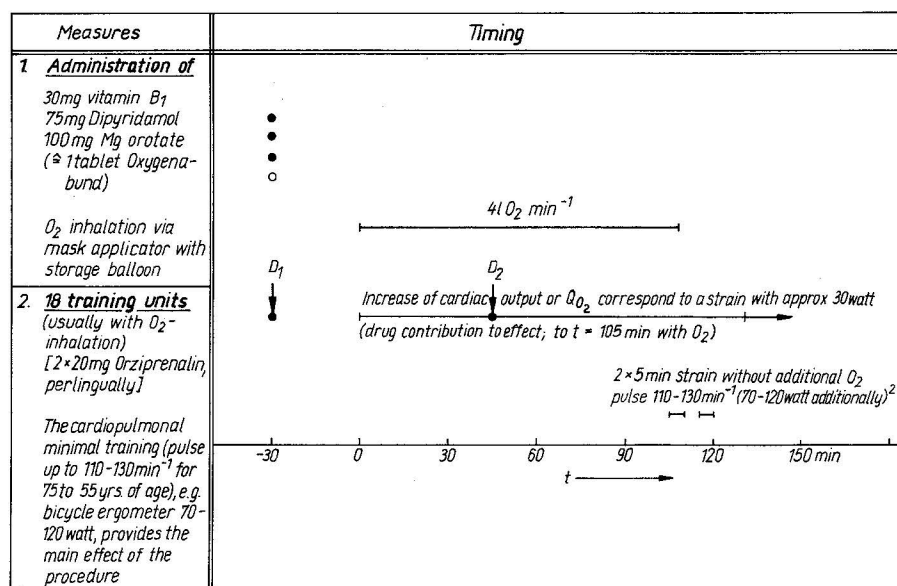


Fig. 230 Program of a treatment unit of the 36 h 18 day O₂MT procedure with increase in cardiac output¹ through a sympathicomimetic drug given before each session, supply of 4 l O₂/min as well as exercise training afterward if at all possible, 10 min with pulse increase to the aerobic/anaerobic border without O₂ inhalation

¹ Contributes to the functional regeneration of the aged heart by permanent improvement of the O₂ offer (QO₂) to the heart in combination with specially designed pharmacological and ergometric training

² As a result of the still existent Orziprenalin action; these figures are about 30 watt lower than otherwise necessary for the strived-for pulse increase

1. Prevention or delay of the occurrence of diseases, illnesses and complaints of old age
2. Increase in physical performance capacity in old age
3. Maintenance of male potency in older age, when combined with specific measures.

Variant GK 4-III: The inclusion of 5 HOT*-UVR treatments and optionally, or measures of the GK 4-II variant into the program of the standard 36 h (18 day) O₂MT procedure, GK 4-I, produces the *intensive variant of the 36 h (18 day) O₂MT procedure* [74]. For the technology, practice and specific effect of the HOT*-UVR we refer the reader to Paragraph 3.3.

The programming of the intensive variant GK 4-III can be taken from Table 29 and Fig. 230.

Indications of the intensive variant GK 4-III are:

1. Severe circulatory disorders in the lower extremities (formation of necroses, pre-amputation stage)
2. Severe cerebral circulatory disorders
3. Efforts to achieve partial rehabilitation in cases requiring care

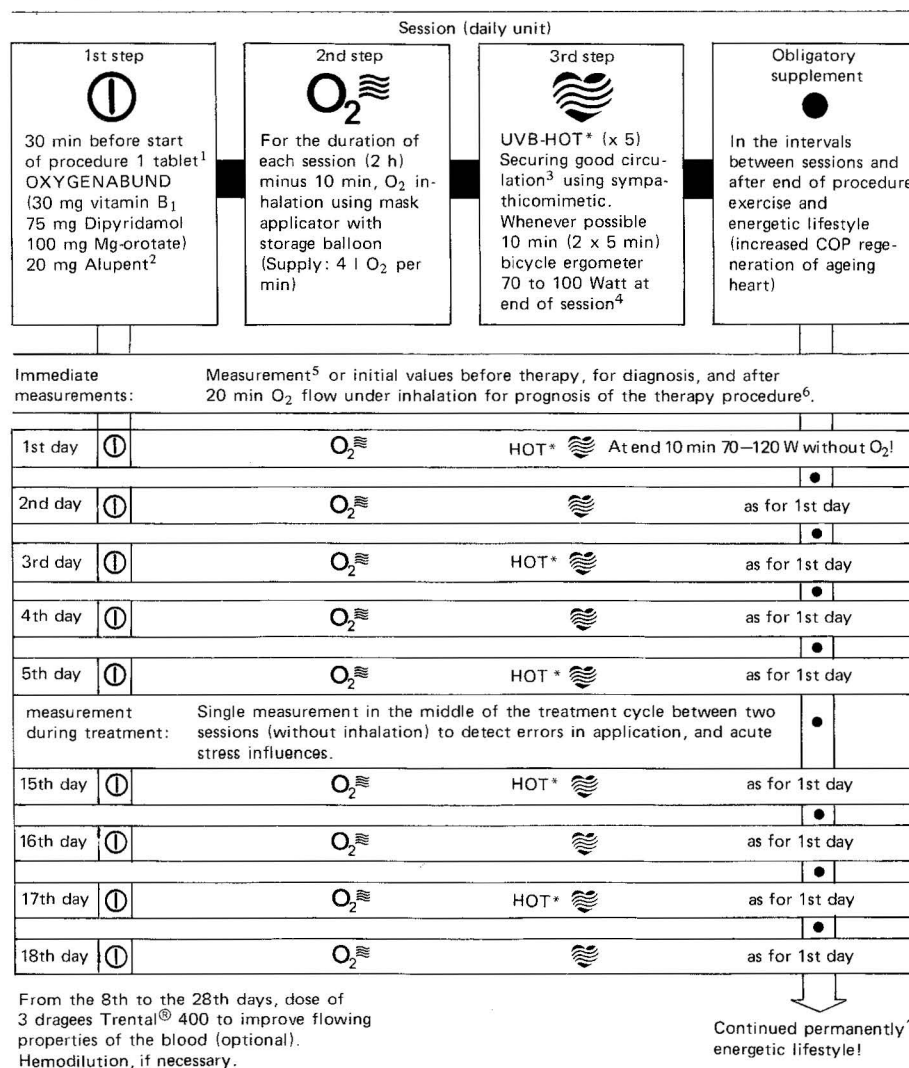
4. Cases with particularly severe O₂ deficiency phenomena (e.g. possible avoidance of coronary bypass operations; variant with 5 HOT* UVR without Alupent and minimal training).

The following results were obtained with the intensive variant in the combat of circulatory disorders in the lower extremities:

1. In stage II (Fontaine) there was generally a *significant increase in the painless walking distance* after treatment with the O₂MT intensive variant.
2. In many stage IV cases partial or total reversals in the necrotic processes could be observed, correlating with a renormalization of temperature in the affected leg, thus *making the already planned amputation unnecessary* (provided that infections did not compel amputation of the diseased leg). In one case of diabetes mellitus, the pretreatment need for insulin disappeared.
3. Long-term stress caused by chronic pain often leads to immobilization or the need for nursing care in stage IV of the occlusive disease. It is precisely these stress factors which form the path to a vicious circle,

Table 29 Variant GK 4-III: Intensive variant of the 36 h 18 day O_2 multistep therapy procedure with lasting effect, with increase in COP and 5 UVB-HOT* treatments. With an additional contribution (according to condition and age) to functional heart regeneration by means of 10 min cardiopulmonal minimal training without O_2 inhalation at the end of each session, with pulse acceleration to the aerobic-anaerobic border. During the

session at 20 minute intervals for 1 to 2 min physical exertion, with a manual ergometer to raise pulse to above 90 per minute (optional)



Cure success measurement⁵: Measurement after end of therapy procedure and training.

Control measurements⁵: After months to years to establish whether a repetition of the procedure is necessary⁸ (repetition after strong stress influences, infections etc.)

¹ If desired, add 1 g vitamin C

² Orziprenalin (Alupent®) 20 mg perlingual. For patients in bad condition, no dose until after 2nd or 3rd session (optional). Take contraindications seriously

³ Whenever possible, the COP to be determined at rest before and after the procedure

⁴ Due to effect of Alupent, these figures are 30 W lower than otherwise necessary for given pulse increase

⁵ Measurement of the arterial and venous peripheral P_{O_2} , at rest and at the same time of day, in blood samples taken from the "arterialized" ear lobe and from the unbound cubital vein, respectively using a special instrument, e.g., Universal P_{O_2} meter, type MO 10, made by VE Kombinat Präcitronic, 8016 Dresden/DDR

⁶ $P_{O_2-art} > 125$ mmHg indicates good response

⁷ Daily dose of Oxygenabund 30 min before exercise causes drop of P_{O_2-ven}

⁸ UVB-HOT* blood-irradiating instrument FMR 10 without blood-foaming, according to G. Wiesner, made by VE Kombinat Präcitronic, 8016 Dresden/DDR

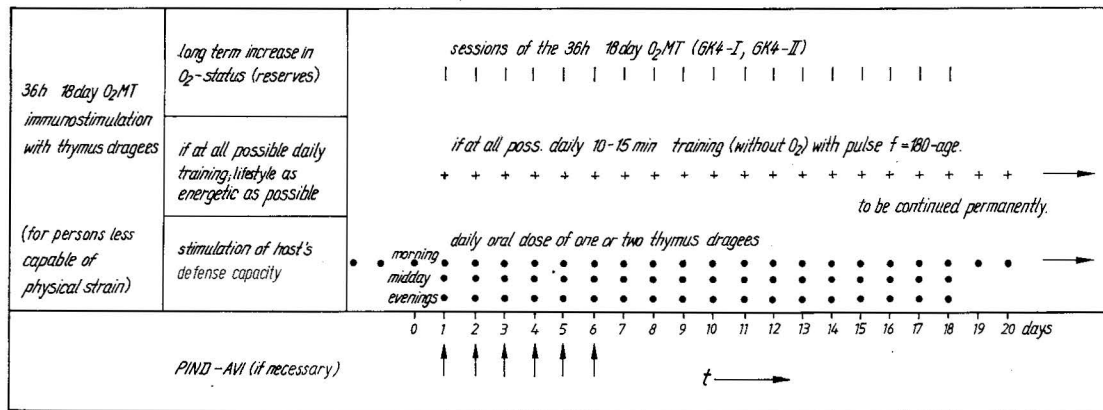


Fig. 231 Treatment schedule of the 36 h 18 day O_2MT immunostimulation variant GK 4-IV. Dosage of thymus dragees (e.g. Thym-Uvocal), Dr. K. Mulli, D-7844 Neuenburg, FRG) continued, 1 dragee daily for a further 30 days. In special cases the immunomodulator PIND-AVI (Inst. of Medical Microbiology, Infections and Epidemic Diseases, University of Munich, FRG) can also be applied, e.g. as follows: 2 mg (1 vial) i.m. per day on days 1–6 (synergetic effect through different effector mechanisms). In addition, the blood glucose level can be increased to $5 \cdot 10^{-3}$ g/ml for 6–8 hours after both treatments on the 17th and 18th days, in order to strengthen the chemotactic attraction of leucocytes to the foci (see text)

which leads to a further drop in the O_2 status. It is very often possible to intercept this circle with the aid of the intensive variant. *Patients who, as severe nursing cases, had put to strain on their environment, left their beds and returned to a life with physical exertion.* In view of the strain that this problem puts on the health and social services, even partial rehabilitation is an important success.

Variant GK 4-IV: The variant of the 36 h (18 day) *oxygen multistep immunostimulation* (O_2MI) results from the combination of immunomodulators (thymus, NeyThymun, PIND-AVI, CEH etc.) with the standard 36 h (18 day) GK 4-I variant or, in cases demanding the greatest efficacy, with the GK 4-III intensive variant. The abbreviation for the first combination is GK 4-IV A and for the second GK 4-IV B.

The programming of the O_2MI GK 4-IV variant is to be taken from Fig. 231 and Table 27 (combination A) or Table 29 (combination B). For the explanation of the immunomodulatory measures, see commentary on the variant GK 2-III.

According to recent research (R.L. Edelson, Columbia University New York), the skin tissue has great functional similarity with the thymus gland (e.g. contribution to the maturing of T-lymphocytes). It can therefore be assumed that an intensification of the microcirculation of the skin by daily hard brushing of the body surface

(3–4 min) causes an improvement in immune defense. Brushing should therefore be considered as a further supplementary measure of this variant.

Indications for the variants GK 4-IV A and B are:

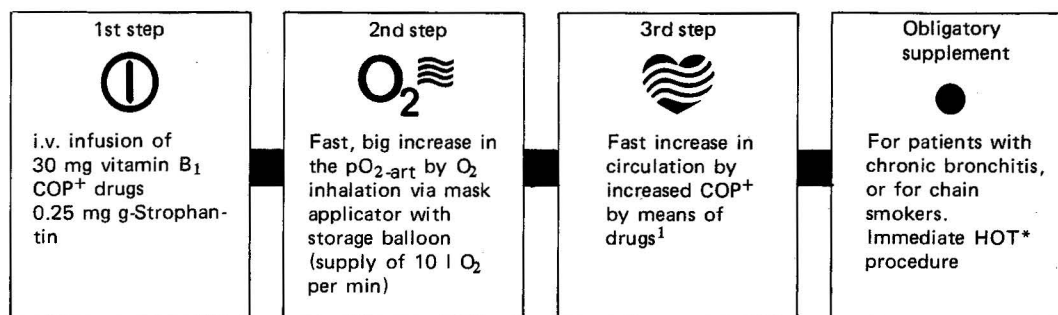
1. Reduction in susceptibility to disease (A)
2. Reduction of the danger of diseases in older age (A)
3. Increase in physical and mental performance capacity in older age (A)
4. Increase in quality of life during chemotherapy and irradiation of cancer (A)
5. Combat of cancer metastasis, reduction of rate of metastasis
6. Immunological cancer therapy (A or B)
7. Combat of cancer (primary tumors and metastases. A or B, if necessary, with 6–8 h increase in blood glucose to $5\text{--}8 \cdot 10^{-3}$ g/ml on the 17th and, if required, also on the 18th, day). Utilization of the standard cancer therapy with surgery, irradiation and chemotherapy plus supplementary threefold application of the O_2MI GK 4-IV; immediately utilizable combination. Pilot treatments using this concept indicated high efficiency.

For 4–7 a threefold implementation of the procedure is generally required (Fig. 280, below).

In rare special cases it can be helpful to include a *juice fast* [350] as a fourth step of therapy in

Table 30 Variant GK 5: O₂ multistep immediate aid procedure with usually lasting effect in crisis (e.g. circulatory disorders, shock, strokes etc.). Variant: without 3rd step for circulation support in high fever

Single process



Increase in the arterial pO₂ as quickly and as greatly as possible by means of O₂ inhalation, as well as in the cardiac output (COP)

Fast bioenergetic triggering of the generalized "cellular vessel wall switching mechanism" of microcirculation when duration of procedure sufficient.

Measurement of O₂
status

After procedure the arterial and venous peripheral P_{O₂} should be measured, at rest. (Blood taken from the earlobe and the unbound cubital vein, resp.)
Determination of O₂ status with η-nomogram.

¹ COP⁺ drugs, e.g. sympathicomimetics such as Mephentermin, Alupent etc. (cf. Table 14)

the variants discussed in this section (cf. Table 42). Clinical fasting should strengthen the therapeutic effect by improving the lung function parameters and the Broca index (Fig. 226) as well as relief of defense functions in the intestinal tract.

For metabolic disorders in the brain (e.g. cerebral arteriosclerosis) we strongly recommend that the O₂MT procedure be supplemented by a 60-day cure with *Pyrrithinol* (Encephabol forte) and calcium antagonists.

4.2.5 Oxygen multistep immediate aid procedure GK 5

The program of the O₂MT immediate aid procedure is presented in Table 30. In order to aid the patients as quickly as possible in acute crises of the most varied kinds, it is important to increase the O₂ supply of the decisive organs as high as possible. The application of pure oxygen alone is often insufficient to fulfil this requirement when the circulatory condition is bad. By inclusion of the further steps named in the table and by the high degree of synergism of the steps involved, and by their simultaneity, an extraordinarily fast increase, or re-increase, in the O₂ uptake of the body tissue is achieved. In addition to the administration of O₂, the i.v. application of sympathicomimetics, for example, in order to increase the COP imme-

diately, also makes a significant contribution. The influx of O₂ can be additionally accelerated by optimizing the 3rd step with drugs to increase COP and, if necessary, by the inclusion of drugs to centralize the circulation, in accordance with Fig. 232.

The given supplementation by immediate HOT*-UVR treatment is worthwhile as its effects (e.g. increase in blood fluidity) set in just a few minutes after treatment. Thorough investigations, lacking as yet, must decide whether it would be worth including the measures named in Table 30 in ambulances.

Examples of indications for the O₂MT immediate aid procedure are:

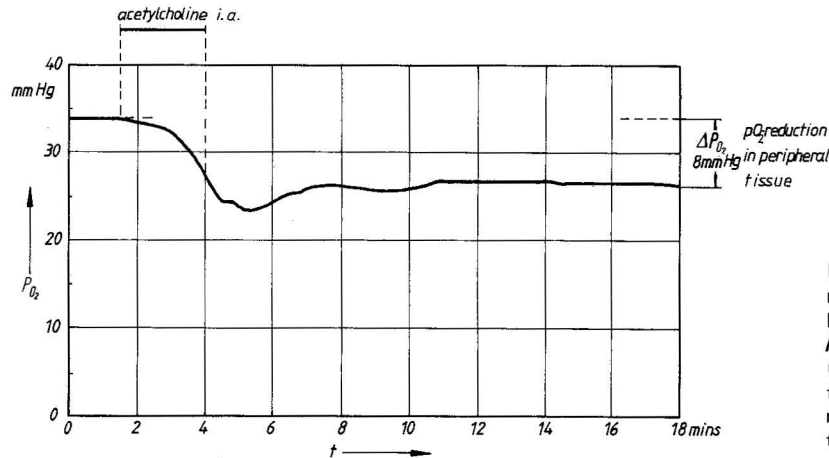


Fig. 232 Small-area PO_2 measurement showing the long-lasting reduction of PO_2 in a peripheral tissue (dog tail) after centralization of the circulation by means of the vasoconstrictor acetylcholine [309]

1. Fast aid in emergencies of all kinds
2. Amelioration of consequences of strokes
3. Combat of shock when still in its reversible early phase
4. Severe concussions of the brain
5. Aid in severe toxic stress
7. Aid in high fever, especially in older patients (also at home).

The supporting of the circulation using O_2 is a standard medical process, especially in anesthesiology. The O_2MT support of the circulation can therefore be seen only as a somewhat increased form of a standard procedure, albeit with greatly extended range of indications.

Figure 233 shows an example of the effect of the O_2MT circulatory support in circulatory stress, by means of $40^\circ C/250$ min whole body hyperthermia. The hyperthermia in a hot water-bath, lasting over 4 h, signified a very great strain on the circulation which even in individuals having an intact cardiovascular system, normally leads to precollapse stages. This is shown in a critical drop in the blood pressure amplitude towards the end of the hyperthermia phase (Fig. 233 A), as we observed in numerous volunteers with former CMT technology [2]. This drop in the blood pressure amplitude does not occur when the O_2MT circulatory support is applied during the phase of hyperthermia (Fig. 233 B). This finding is to be expected from the viewpoint of the physiological bases, because, as already shown in Fig. 124, a significant reduction in the O_2 saturation of the blood occurs with an increase in temperature from 37 to $40^\circ C$ or higher, especially in older persons. It is therefore very obvious that the O_2MT circulatory support should be applied during attacks of fever (even at home), when

weakened or old patients are affected. The fast fulfilment of this demand will frequently prove to be life-saving. As the febrile episodes usually last only a few hours, O_2 provision from small, portable pressure cylinders is generally sufficient here.

The optimization of the O_2 supply to the brain before and during major operations is a very important indication. In order to achieve re-synthesis of energy-rich phosphates, adequate for the situation, it does not suffice to begin artificial respiration with additional O_2 10 minutes before the operation, as is generally the case today. Our experiments with laboratory animals [4] have shown that, in order to achieve maximum recycling of energy-rich phosphates in the brain, O_2MT circulatory support should begin 120 min before the start of the operation. Measurements in experiments with laboratory animals of the drop in the concentration of energy-rich phosphates after the end of the O_2MT procedure (cf. Fig. 133) have shown that, even after 4 h, the level of ATP is still 10% above the normal level. The stabilizing effect on the metabolic O_2 requirements of the brain, the maintenance of the functional stability of the blood-cerebrospinal barrier and the achievement of a sufficient clearance function for acidic metabolites by an O_2MT -stabilized circulation, should therefore last for some hours after the end of the procedure.

It is to be concluded from impressive case reports [351] that the consequences of acute cerebrovascular insufficiencies can be ameliorated if the O_2 situation is improved, using this variant, as soon as possible after the onset of the circulatory disorder, especially before manifestation of the consecutive perifocal brain

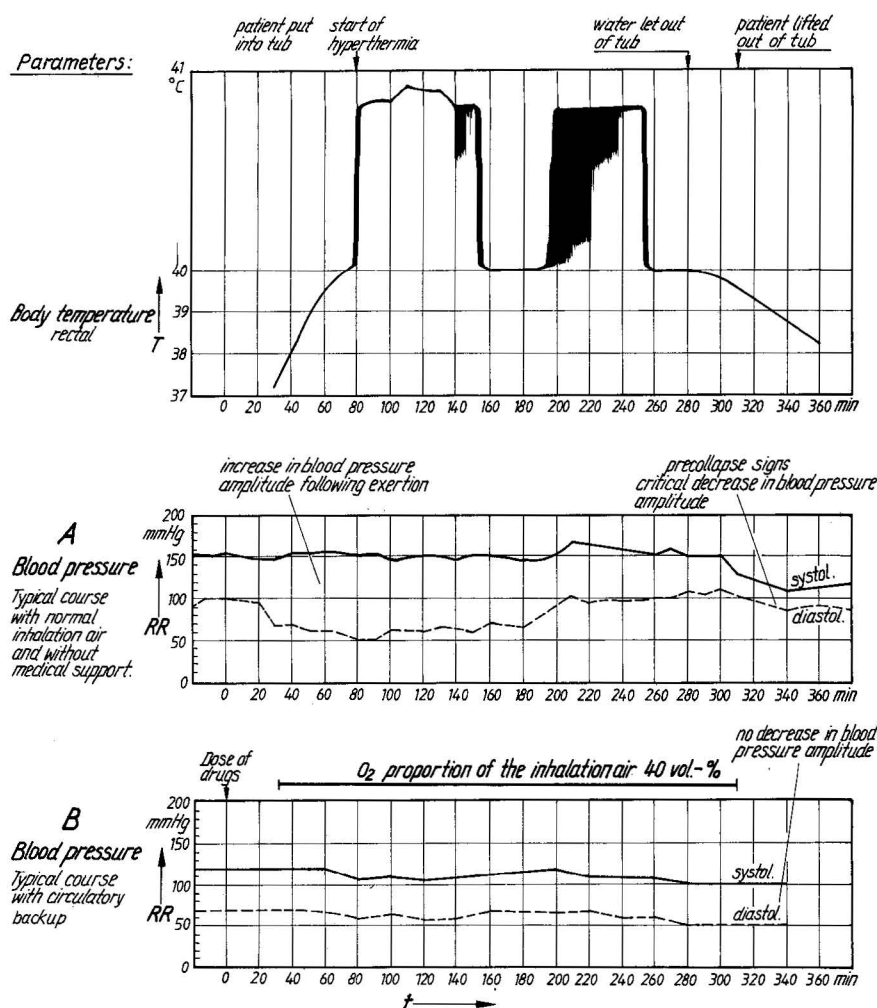


Fig. 233 The effect of circulatory backup by means of O₂MT after circulatory disorders due to a 250 min 40 °C whole body hyperthermia

edema. Such findings encourage us to hope that the consequences of transitory cerebral ischemia can be weakened in this way. In the first few weeks after severe cerebral circulatory

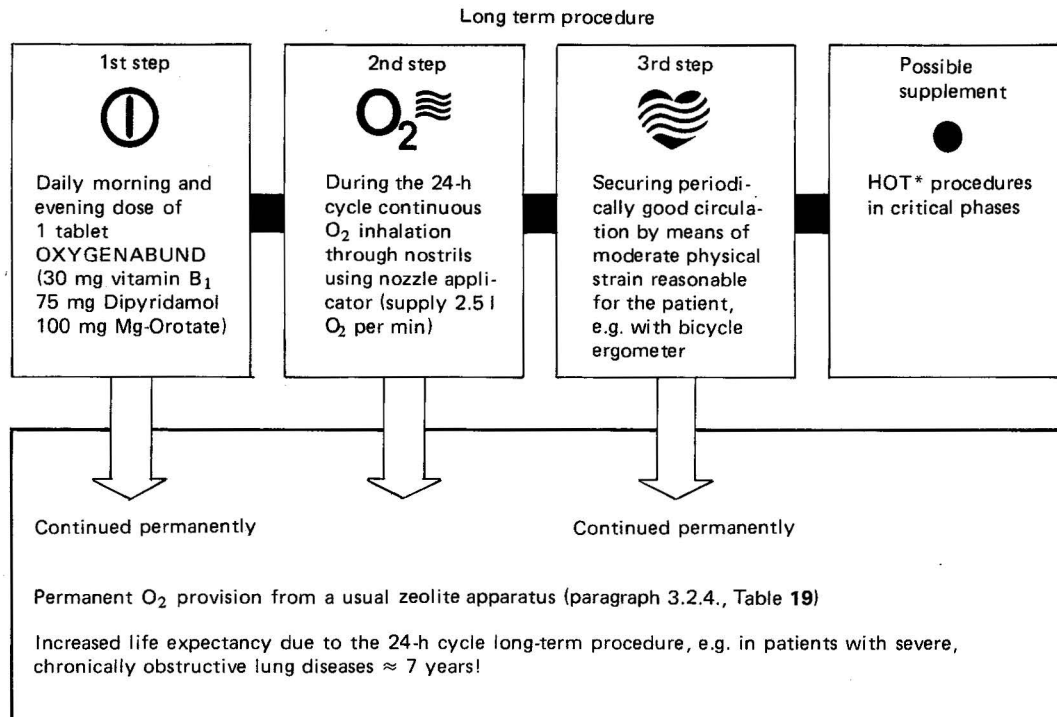
disorders and cerebral ischemia it should also be attempted to strengthen the tendency to restitutio ad integrum, e.g. by O₂MT sleep and supplementation by HOT*.

4.2.6 Oxygen multistep long-term aid GK 6

The program of the O₂MT long-term aid [2, 4, 352, 353] can be seen in Table 31. The characteristic of this variant is that an O₂ flow of approximately 2.5 l/min is given to the patient for very long periods and, most importantly, without intermissions over the 24 h daily cycle, using the comfortable nozzle applicator or mask applicator of soft synthetic material (with storage balloon). The specific feature is that the O₂ status is further raised by taking 2 Oxygenabund tablets daily (1st step) and moderate regular exertion.

Examples of indications for the O₂MT long-term aid procedure are:

1. Partial respiratory insufficiency: chronic obstructive and chronic inflammatory lung diseases, degenerative loss of function, infectious lung diseases, postoperative conditions such as lobectomy and pulmectomy, formation of thickenings, cicatricial scars, permanent shortness of breath [354, 355]
2. O₂ deficiency diseases: ischemic diseases of organs such as heart and brain, or of functional units of organs such as gastrointestinal tract or the sense organs
3. Long-lasting unconsciousness (cf. also Paragraph 4.2.3, aid for resuscitation)
4. Intensive nursing cases.

Table 31 Variant GK 6: O₂ multistep long-term help. Help for patients with critically reduced lung function¹

Follow up: First, measurement of the pO_{2-art}, at rest, e.g. once to twice a month.
 Level to be attained under O₂ inhalation = 70 to 80 mmHg (9.8 to 10.6 kPa)

¹ In such patients, the diminished effective breathing time (12 instead of 24 h a day) means that life expectancy is significantly reduced

The approaching ability to draw additional O₂ from devices driven from mains electricity adds a new field of great breadth to the health service. It is the provision of immediately felt technical help, as in Fig. 234, in the patient's own home, in a restroom or bedroom or, for example, in old people's homes for the many individuals with critically reduced lung function, or for those whose quality of life is often drastically reduced. Permanent help of this sort is also indicated for the very large number of patients who suffer from acute O₂ deficient conditions and O₂ deficiency diseases, as a result of a drop in cardiopulmonary performance. From the viewpoint of the physiological foundations we are justified in hoping that it will be

possible to alleviate the complaints and diseases of these people even in such cases, and thereby to improve their quality of life in a way that today can hardly be overestimated.

This variant with its supplementation appears to be particularly indicated for intensive care after severe craniocerebral traumas with long unconsciousness. In connection with this we would remind the reader of supplementation by HOT*-UVR treatment.

One of the most important tasks of the medical-technical industry is to extend the present production of zeolite devices as quickly as possible to a large scale and with low prices, so that the long-term help discussed can soon be widely offered to both groups of patients named.



Fig. 234 Lasting aid for patients with critically reduced lung performance by means of a small easy-to-wheel zeolite device (daily change of position between bedroom and living room); amelioration of difficult breathing (Photo: Drägerwerk, Lübeck/FRG)

4.2.7 Oxygen multistep hyperbaric quick procedure GK 7

The oxygen program of the O_2MT hyperbaric quick procedure is roughly the same as that given in Table 25, for the normobaric 15 min O_2MT quick procedure. According to the case in question, there is physical exertion using a step-climbing system, a home trainer, a running belt or manual ergometers inside the room. The excess O_2 pressure with simultaneous strong physical exertion (cf. Fig. 174 and Paragraph 3.1.5) and, if necessary, HOT*-UVR treatment

and hemodilution [47] before the start of the hyperbaric treatment, provides a most *intensive variant for severe cases* (e.g. microangiopathias in diabetics), which justifiably gives us great hope for the future. The extent and limits of the effects of this new method, and its specific indications, are still unknown. Research with this interesting, but complicated variant was begun at the end of 1986 by Fischer in Nordrach-Klausenbach (FRG) and in our Institute.

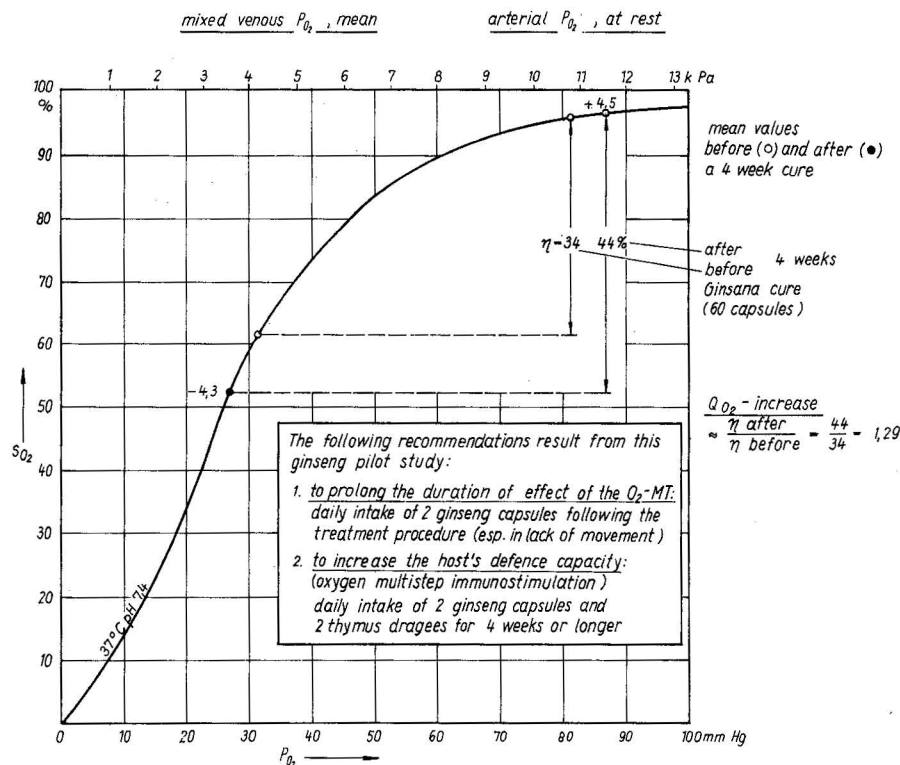


Fig. 235 Improvement of the P_{O_2} values in blood and of the arteriovenous saturation difference η by means of daily uptake of 2 capsules Ginsana®, G 115¹ (200 mg standardized ginseng extract) over 4 weeks or permanently. N = 10 volunteers (8 ♂, 2 ♀) from the working population with an average age of 49.9 years

¹ Pharmaton SA, CH-6903 Lugano, Switzerland

4.2.8 Further developments and simplifications of the oxygen multistep therapy or oxygen multistep immunostimulation

In the previous paragraph we discussed a further development of the O_2 MT procedures towards the greatest strength of effect. The further development with the aim of making the basic procedure as simple as possible with moderate, just sufficient strength of effect and with as little effort as possible, is also of great significance for the health service, however. The variant of 15 min O_2 MI, GK 2-II, easily performed on an outpatient basis, e.g. with physical exertion using the step-climbing method and with oral administration of thymus dragees or NeyThymun drops, already lay along these lines. Further simplifications would have to be worked for in order to introduce a prevention procedure against diseases and, most importantly, or general cancer prophylaxis.

Drugs, or combination of drugs, which measurements show to improve the O_2 status long-term, are of great interest here. It is obvious that such substances should be sought in the spectrum of drugs for geriatrics. We were led to the ginseng extract G 115 [356] because Schimert (a pupil of von Bergmann, and former director of the Institut für Prophylaxe der Kreislaufkrankheiten, University of Munich, FRG) measured an increase in the maximum O_2 uptake of 21 % in competitive sportsmen with this preparation compared with an equally trained control group with placebo [357] in a double-blind study.

The similarly positive results of our ginseng pilot study with 10 volunteers and with 4 weeks

of oral administration of 2 Ginsana G 115 capsules daily, is summarized in Fig. 235. The $P_{O_2\text{-ven}}$ at rest, was reduced by the ginseng

preparation by 4.5 mmHg (0.5 kPa). The η -value therefore rose from 34 to 44%. The oxygen offer Q_{O_2} to the body tissue in the healthy volunteers (average age 49.8 yrs) rose from 100% before the cure to 129% afterwards. This is a very positive finding, just like the result quoted from [357] as to the increase in the maximum O_2 uptake in sportsmen from 100 to 121%. We would remind the reader here (see Paragraph 1.1.5.3) that in healthy volunteers an improvement in the O_2 offer, at rest, Q_{O_2} from 100% before O_2MT to 133% afterwards was found (and in patients in need of therapy, from 100% before to 230% afterwards).

Studies are under way with 8 weeks of a daily dose of 2 ginseng capsules and with a larger number of volunteers. Studies using other substances, such as Almitrin or Yoctation (250 mg, daily for 3 weeks) [358] etc., and with combinations of substances, are planned.

Whether the measured improvement in the O_2 status, attainable for weeks using drugs, combined with the immunomodulation using thymus dragees or similar preparations, is already sufficient for a general cancer prophylaxis, remains to be discovered by future research. This form of *prophylaxis* simply by the oral administration of a combination of drugs is in any case a dream target, for which it is worth researching. The 6-week ginseng-thymus cure discussed should already be sufficient to achieve less high-flying goals, such as the reduction in the frequency of infections, etc.

4.3 Body section variants

4.3.1 80 min oxygen multistep nicotinic acid procedure KA 1

The program of the 80 min O_2MT nicotinic acid procedure [105, 360] is summarized in Table 32. A speculative working hypothesis and simple energetic considerations [105] led the author to the discovery of the O_2MT procedure for the head and neck region in 1972. With it vasodilation specifically in the head and neck region is brought on by administration of a high dose of nicotinic acid during the effects of the 1st and 2nd steps of the O_2MT . This stronger circulation is also visible externally in pronounced reddening of the face, the flush effect. This effect is particularly strong when the nicotinic acid is taken on an empty stomach, and lasts about 60 min. The improvement in brain circulation, which is also desired, can of course be supported by the infusion of high molecular weight dextran.

Examples of the indications for the 80 min O_2MT nicotinic acid procedure are:

1. Regulatorily conditioned orthostasis in hypotonia
2. Morbus Ménière
3. Hemicephalgias outside the Ménière complex
4. Transitory ischemic attacks (TIA)
5. Functional disorders of the optical sense (dysopsias), presumably due to insufficient circulation.

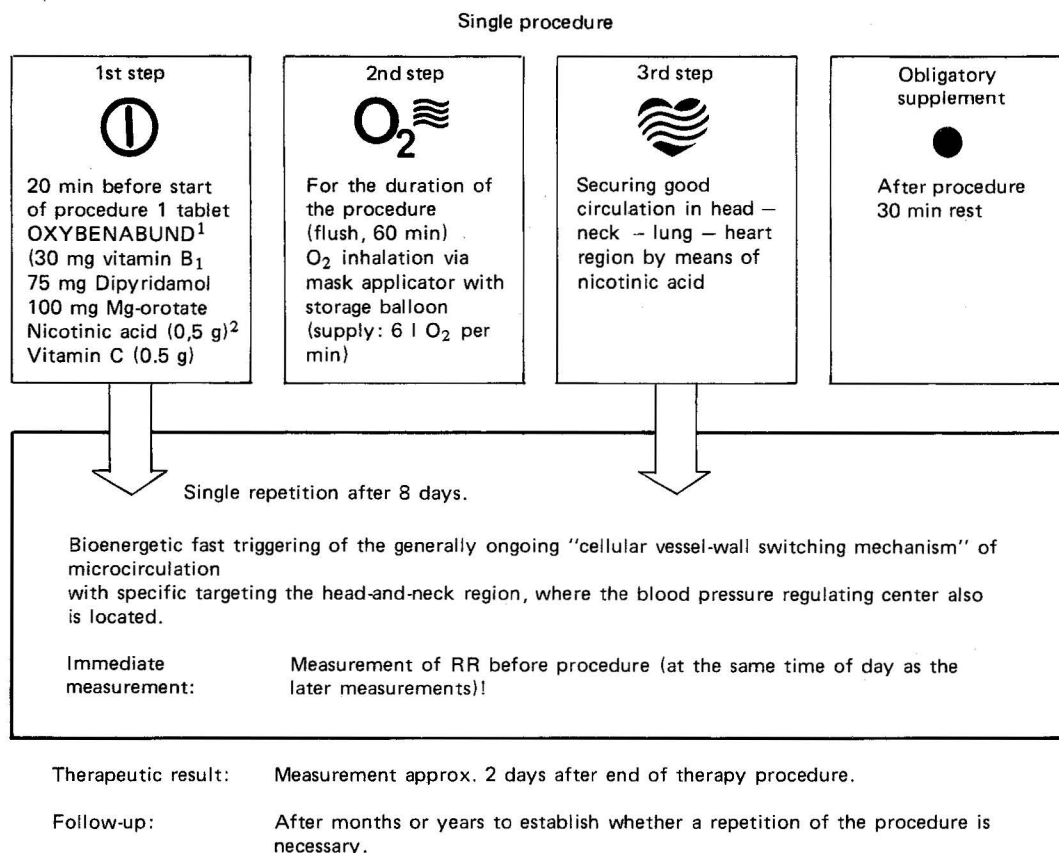
When applied against regulatorily conditioned hypotonia, this variant achieved increases in the blood pressure amplitude and orthostatic response in a very high percentage of cases,

lasting months and even many years, increases which have not so far been achieved with such quality and duration in any other way. There are few medical therapies so short and simple, that produce such a great change in the patient's well-being, surprising both patient and doctor. It is therefore almost incomprehensible and very regrettable that this procedure has only been used rarely so far and has remained fairly unknown, despite the fact that it was published in a respected medical journal as long as 14 years ago [360].

This procedural variant also forms the key to the extremely effective combat of Ménière's disease. Pilot treatments in Dresden showed that previously regular Ménière attacks remained fully absent due to O_2MT procedure with nicotinic acid. How many Ménière patients could have been spared the loss of hearing in 1 year if this new therapeutic method had been recognized and acknowledged by the responsible medical practitioners 13 years ago!

It seems methodologically reasonable to enlarge the COP, the RMV and, correspondingly, the O_2 flow by means of physical exertion during the flush effect. This thought leads to a combination of the O_2MT nicotinic acid procedure with the O_2MT quick procedure. This combined procedure represents an intensive variant of both the O_2MT quick procedure GK 2-I and the O_2MT nicotinic acid procedure KA 1. Because of the extreme exertion connected with

Table 32 Procedure for the head-and-neck region against regulatorily conditioned hypotonia. Programming of the 80 min O₂ multistep nicotinic acid procedure with lasting effect. Variant: combination of KA 1 + GK 2-I to intensify the quick procedure in the head-and-neck, lung and heart region



¹ On an empty stomach

² Such high doses of nicotinic acid cause a deprivation in metabolic methyl donors. Therefore, a supplementary lecithin preparation should be administered at the days of treatment

it, this combined procedure can only be used on patients whose circulatory condition is good. In connection with this we should refer to single observations of euphoric sensations lasting several days.

The patient must always rest for approximately 30 min, in a lying position, after O₂MT nicotinic acid procedures.

4.3.2 Oxygen multistep supplementary procedure KA 2

The *program for the O₂MT supplementary procedure* [260] is summarized in Table 33. In order to combat local circulatory disorders the most important undertaking is to increase the O₂ uptake, at rest, or the utilization factor η of the O₂ binding capacity of the blood to as high a level as possible and for as long as possible, by means of the O₂MT procedure. This increase alone is often sufficient to

achieve the bioenergetic high-charging of the blood microcirculation in the tissue areas with circulatory disorders. The probability of crossing the threshold to the triggering of the switching effect is increased if the supplementary procedure follows as soon as possible. This O₂MT supplementary procedure against local circulatory disorders emphasizes the design of the 3rd step and its adaptation to the conditions

Table 33 Variant KA 2. O₂ multistep supplementary procedure for the GK 2-I or GK 4-I variants. Programming the procedure against local circulatory disorders

Supplementary procedure			
1st step  30 min before start of procedure 1 tablet OXYGENABUND¹ (30 mg vitamin B₁ 75 mg Dipyridamol 100 mg Mg-orate) and drugs for the 3rd step	2nd step  Throughout the procedure O₂ inhalation with a mask applicator with storage balloon (supply: 10 to 30 l O₂/min, according to exertion)	3rd step  Increased cardiac output and thereby circulation by physical exertion² reasonable for the experimental (20–150 W) e.g. with bicycle ergometer or circulation centralization by means of dihydroergotamine or pholedrin etc. Vasodilation in O₂-deficient region by means of drugs or local hyperthermia (see Table 16)	Possible supplement  HOT* procedures Especially indicated for circulatory disorders in the lower extremities
Bioenergetic triggering of the "cellular vessel-wall switching-mechanism" of microcirculation in tissues with circulatory disorders. Immediate measurement: Large-area P_{O₂} measurement in this tissue and temperature measurement before treatment.			

Measurement approx. 2 days after end of treatment, of the tissue pO₂ as well as tissue-temperature.

¹ If necessary, also 1 g vitamin C

² Exertion such that pulse $f \approx 180$ -age

of the individual patient. It is the task of the 3rd step here additionally to increase the blood flow specifically in the tissue with circulatory disorders. To achieve this a series of measures are combined, given in the table under step 3. Among these are the general increasing of the COP, the redistribution of the blood volume to target areas by means of certain drugs, and the reduction of the hematocrit in order to increase blood fluidity. These measures with a generalized effect are balanced by local pharmacological measures and measures with local or regional hyperthermia.

In local circulatory disorders (e.g. in angio-organopathias) there is often a considerable reduction in the mean pH in the tissue with O₂ deficiency, caused by the formation of lactic acid, which can be recognized by the onset of severe pains [210]. We must therefore reckon with an intensification of the circulatory dis-

order due to the drop in blood microcirculation as a consequence of a reduction in the flexibility of the red blood cells (feedback). From this viewpoint it is not surprising that dramatic improvements in disturbed circulation were observed due to increasing of the flow properties of the blood, especially when there is reduced pH, e.g. by i.v. administration within 1 min of $4 \cdot 10^{-5}$ g/kg O-(β -hydroxyethyl)-rutoside, Venoruton, from Zyma-Blaes, Munich, FRG [114]. The high degree of the improvement obtainable can be explained by the fact that the object of therapy here is a typical system with feedback. At this point we would like to emphasize the alleviation of peripheral circulatory disorders by means of hemodilution with plasma expanders [47], and by means of 3,7-dimethyl-1-(5-oxo-hexyl) xanthin (Pentoxifyllin, Trental) [263]. This improvement in the fluidity of the blood is obligatory with the KA 2 variant.

5. Areas of oxygen multistep therapy application

5.1 General aspects

5.1.1 Medicine and physiology

We are experiencing the dawn of that great time when medicine and the basic disciplines of the exact sciences will form an ever-closer alliance for the good of mankind. A sign of the approaching change is the avalanching penetration of physics, mathematics, biochemistry and technology into many branches of medicine. The change towards exact science is very advanced in *physiology*. In the same way as Otto Warburg introduced a quantitative working method into cell physiology half a century ago [362], human physiology today stands on a firm foundation of measured values and mathematically defined regularities [32]. Physiology therefore now stands at the forefront of the struggle for progress in medicine. The enormous complications of this process have as yet been grasped by only a few medical practitioners: how else can we explain the broad gulf that often yawns between the results of physiological research and their creative utilization in the health service?

It is particularly noteworthy for our subject that leading physiologists have recently placed the recognition of the *key role played by the oxygen metabolism of the tissue (energy provision) for the living organism* at the centre of their work. Eight international symposia on the transport of oxygen to tissue have already taken place: 1977, 1978, 1979, 1980, 1982, 1984 [162, 169]. These symposia have so far been mainly attended only by physiologists, and interdisciplinary conclusions for the combat of diseases have only rarely been drawn from the results. This monograph has therefore attempted to build a bridge between a current field of physiological research and the practising doctor.

Apart from the contents of this book, we only wish to name the following examples of the progress in the health service that could result from the creative connection of the results of physiology with clinical medicine, linked with our theme:

1. Research into regional lung function with the uneven distribution of alveolar ventilation and blood perfusion in the lung tissue; the resulting knowledge of the influence of gravity on the distribution of air and blood in the healthy and diseased lung, as well as the consequent insight into the dependence of the pulmonary gas exchange on the body position. By translating these results of respiratory physiology into practice (West [83, 363, 364]), significant progress in intensive care has been achieved and countless patients with respiratory diseases have been helped.

2. Research into the mean dependence of the arterial PO_2 , at rest, on age (Loew and Thews [85]) stimulated the development of devices to enrich the inhalation air with oxygen, which can also be used in the patient's home [285]. The same physiological research led to questions following the unexpected discovery (1977/82) of the switching mechanism of the blood microcirculation, governed by the PO_2 at the venous capillary end. The utilization of this mechanism, which works in a generalized way in the whole body, allows an increase in the O_2 status, fallen due to old age and stress, for months up to years to levels that existed during youth, with the aid of the O_2 MT.

3. Research into the inhibition of the microcirculation at the transition from normal pH 7.3 to pH 6.7 at the capillary/venule boundary in glycolyzing tissue (stiffening of the red blood cells, sticking of leucocytes, tumescence of the endothelial cells, leakage of the capillary wall with escape of plasma and aggregation of red blood cells etc.) [114, 120, 140, 146, 171, 365] resulted in fundamental aspects for the selection of the drugs and the time of administration in the combat of myocardial infarction [122, 148, 366, 367] and cancer [22, 23, 121, 124, 136, 368].

5.1.2 Symptoms and causes of disease. Combat of falling ill

Most prophylactic and therapeutic measures today still aim to influence symptoms recognized in complex systems of the living organism, and their control. Future medicine will not so much be concerned with only the *symptoms of diseases* in this way, as with applying itself against the *causes of the diseases*, supported by measurement, calculations and biomedical technology. The common causes of the diseases and potentially fatal crises lie, much more often than generally thought today, in deficiency conditions (energy deficiency, usually caused by O_2 deficiency) with alterations of the cells or cell organelles of the organism and its organs. *The temporary or lasting positive influence of the metabolism of the cells, in conjunction with biotechnical means and controls, therefore represents a weapon of fascinating universality against large groups of diseases and crises.*

A particular important example of the utilization of this principle for health care is the combat of the many O_2 deficiency diseases and crises which not only occur in older age, but also as a consequence of environmental conditions that are constantly deteriorating (lack of exercise, stress, air pollution) and becoming very much more significant. The different variants of the O_2 MT discussed form a specific tool against these. Despite its very great efficacy, however, this tool is as yet only slightly acknowledged and applied.

Moderate arterial hypoxemia, such as is observed in bed-ridden or paralysed patients with sound lungs, for example (extreme lack of movement), also has great pathogenetic significance: to begin with, the relative slight hypoxemia is disguised by circulatory and ventilatory compensation mechanisms. This results in local vasodilatation in the most important organs, increased cardiac output (COP) and intensified ventilation, in order to secure a sufficient delivery of O_2 . The coronary vasodilatation is of critical significance here. If the increase in COP is insufficient, a further deterioration in the hypoxidosis occurs, which most affects the myocardium and the brain. The vicious circle is clear. In such cases, therefore, even slight reductions in the O_2 offer to the body tissue (reduction in the product $\eta \cdot \text{COP}$), which neither lead to cyanosis nor, as a rule, are defined as arterial hypoxemia, are often dangerous [92]. This is particularly the case when there are only slight cardiac performance reserves. The consequences are, at first, hypertonia, tachycardia and, later, hypotonia. The O_2 MT is strongly indicated if these symptoms appear.

The real field of application of O_2 MT lies long before the combat of diseases and crises: it is the *prevention of falling ill, by maintaining a high level of energy provision for the organism and its defense system throughout the whole of human life.*

5.1.3 The four temporal effects of the oxygen multistep therapy

1. Effect during the procedure. Particularly strong effects during the procedure are to be expected where the O_2 -enriched respiratory gas or the increased $PO_{2-\text{art}}$ (cf. Fig. 7) work out directly (not weakened by the typical course in the upper part of the HbO_2 dissociation curve). This applies to the alveolar system of the lung, for the artery walls, for the lens of the eye, i.e. to systems where the *pressure gradient of the O_2 diffusion is mainly determined by the arterial PO_2* . The other direct effect during the procedure is the *increase in the PO_2 , even at and near the venous end of the capillaries* (cf. Fig. 3).

The previously mentioned improvements in the PO_2 levels have long been utilized as *momentary effects* within the framework of the standard measures of O_2 application in medicine (intensive care units, emergency service, combat of

acute O_2 deficiency crises, prophylaxis of shock, long-term help for patients with advanced lung insufficiency etc.). An important momentary consequence of the rise in the O_2 status is a significant *rise in physical performance capacity*, which measurements show to increase during the procedure. The increase enables the patient to undergo physical exertions during the procedure, which he would often be unable to do without O_2 support (e.g. O_2 MT quick procedure, O_2 MT obstetrics procedure). This rise in physical performance capacity also makes it possible to *achieve physical performances in the short intervals between the individual sessions, which the organism normally cannot or can no longer achieve* (O_2 MT short procedure).

These momentary effects must be strictly distinguished from the *integral effects*, which are

the most important part of the O_2 MT as they alone bring about the effects which endure long after the end of the procedure. The high-charging of the blood microcirculation by the reversal of the endothelial cell swelling, which has occurred in hypoxia, is of prime importance here. The momentary effects during the procedure end to some extent in a *functional regeneration of the systems or organs* (lungs, heart, vascular system etc.).

2. Fading effect after end of procedure. The fading effect was discovered in 1971 when energy-rich phosphates (ATP, CP) were measured in the brains of rats [4]. It was found that the ATP and CP concentrations rose after 90 min O_2 MT treatment from 100 to approximately 165 %, and only faded to approximately 112 % 180 min after the end of treatment (cf. Fig. 133). This method to induce the resynthesis of energy-rich phosphates for some hours has been clinically used in major brain operations in Dresden. This improved provision of energy immediately before foreseeable severe stress (operations, births, special performances by singers, politicians etc.) could in future be an aid which is also strongly felt subjectively.

3. Immediate effect of the lasting, great increase in the O_2 status. We define as *immediate effects* those lasting increase in the O_2 uptake of the body tissue and in the CO_2 production, and their consequences, which are measured or observed after a successfully completed O_2 MT procedure. It almost goes without saying that these immediate effects are stronger, the worse the initial O_2 status (the higher the age and

the more pronounced the deterioration in status due to stressful influences). Typical examples of frequently reproduced immediate effects are: increased circulatory stability, elimination of orthostatic symptoms in hypotonia, drop in the — mainly systolic — blood pressure in essential arterial hypertonia (stages I and II, WHO), drop in blood sugar levels in senile diabetes, combat of migraine, Morbus Ménière, Ménière's syndrome and hemicephalgias of unknown origin, night-time cerebral ischemias with disturbances of the sleeping-waking rhythm¹, reduction in the visual and acoustic reaction time, subjectively felt improvement of many symptoms of chronic IHD (= ischemic heart disease), reduction in the activities of dystrophic enzymes in damage of the liver parenchyma, elimination of dysopsies, increase in body defense system, general increase in vitality, and the lasting, measurable increase in the physical performance capacity (double blind study [61]).

4. Long-term effects of the lasting, great increase in the O_2 status. *Long-term effects* are the result of maintaining an O_2 supply to all tissues, organs and systems of the organism consistently above the expected level over a period of years and decades, using O_2 MT. The time since the discovery of the lasting effect of the O_2 MT (1977) is too short to allow definite statements on this important question. A growing number of individual observations point to a postponement of physiosclerosis and of the ageing of the skin. The next paragraph discusses the reasons that justify our hope that human life can be prolonged and made worth living for longer by the maintenance of a high O_2 status with as few interruptions as possible (frequent PO_{2-art} control measurements, O_2 MT as soon as a reduction is ascertained).

¹ The change from waking to sleeping (and vice versa) is an energy-requiring (O_2 -requiring) process

5.1.4 Stimulation of defense against diseases and reduction of their danger in old age as ways to approach the maximum biological age of the human organism

The aim of the O_2 MT is to influence positively the life of the individual by the application of variants adapted to his needs. Figure 236 gives examples of the human life-span with various pathogenetic disturbing factors. Positive influence means the *reduction of the frequency and danger of illnesses, increased life expectancy and an increase in vitality and hence also in the physiological age*. In this goal we see no contradiction to efforts to limit the population of our planet. Great progress for society can

always flourish when the experience and wisdom of the old combine with vitality and creative power.

According to Fig. 236 the genetic program of the human organism should not lead to death before the age of 120 years [369]. In reality, the pathogenetic disturbing factors and their simultaneous occurrence in the late phase of life in the framework of polyopathias cause a much earlier end to life. To supplement our presentation we can include a result gained by

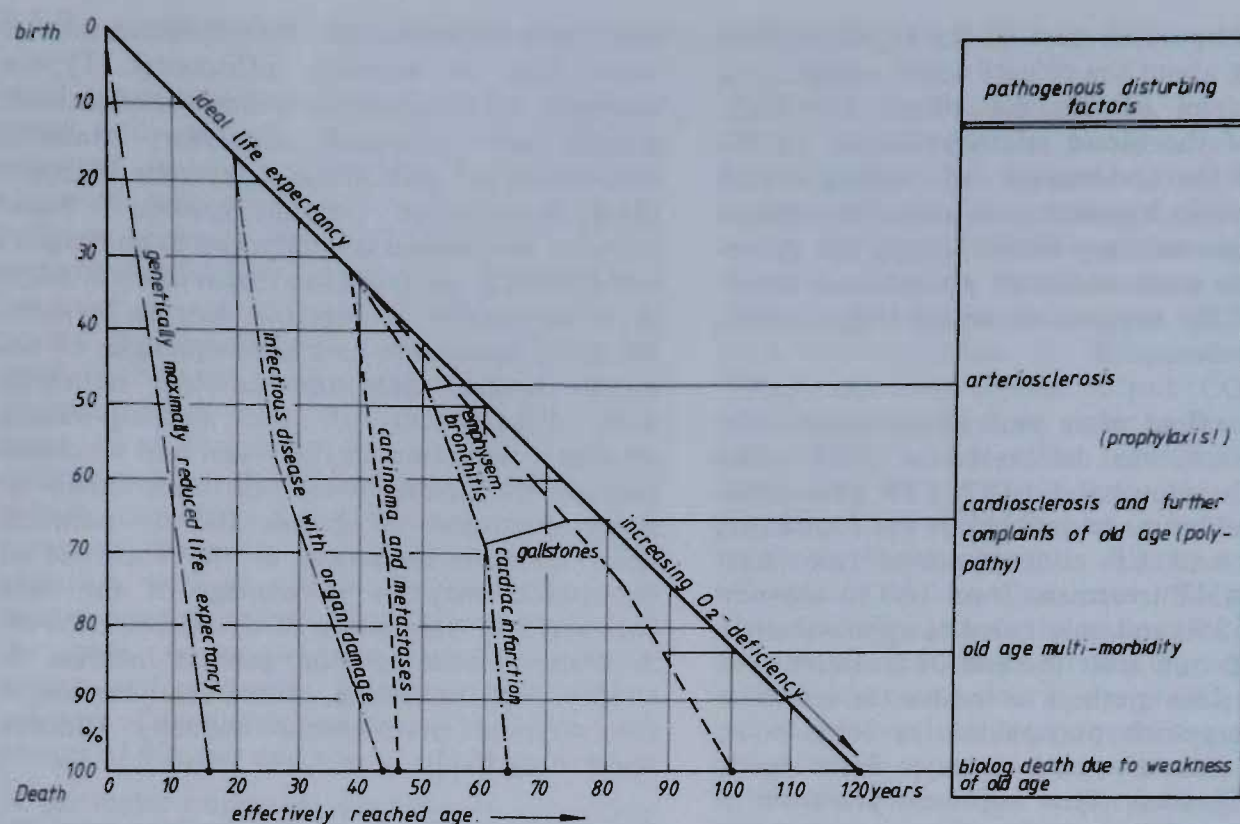


Fig. 236 Influence of various pathogenic disturbing factors on the human life span [276]. Recommendations to preserve fitness: gymnastics (6–18 years of age); sports, regular exercise training every 2nd or 3rd day (18–50); O_2 multistep immunostimulation, O_2 MT: GK 2-II variant (50–75); O_2 multistep immunostimulation, O_2 MT: GK 4-IV variant including regular physical activity (75–90); O_2 MT permanent aid GK 6 (> 90)

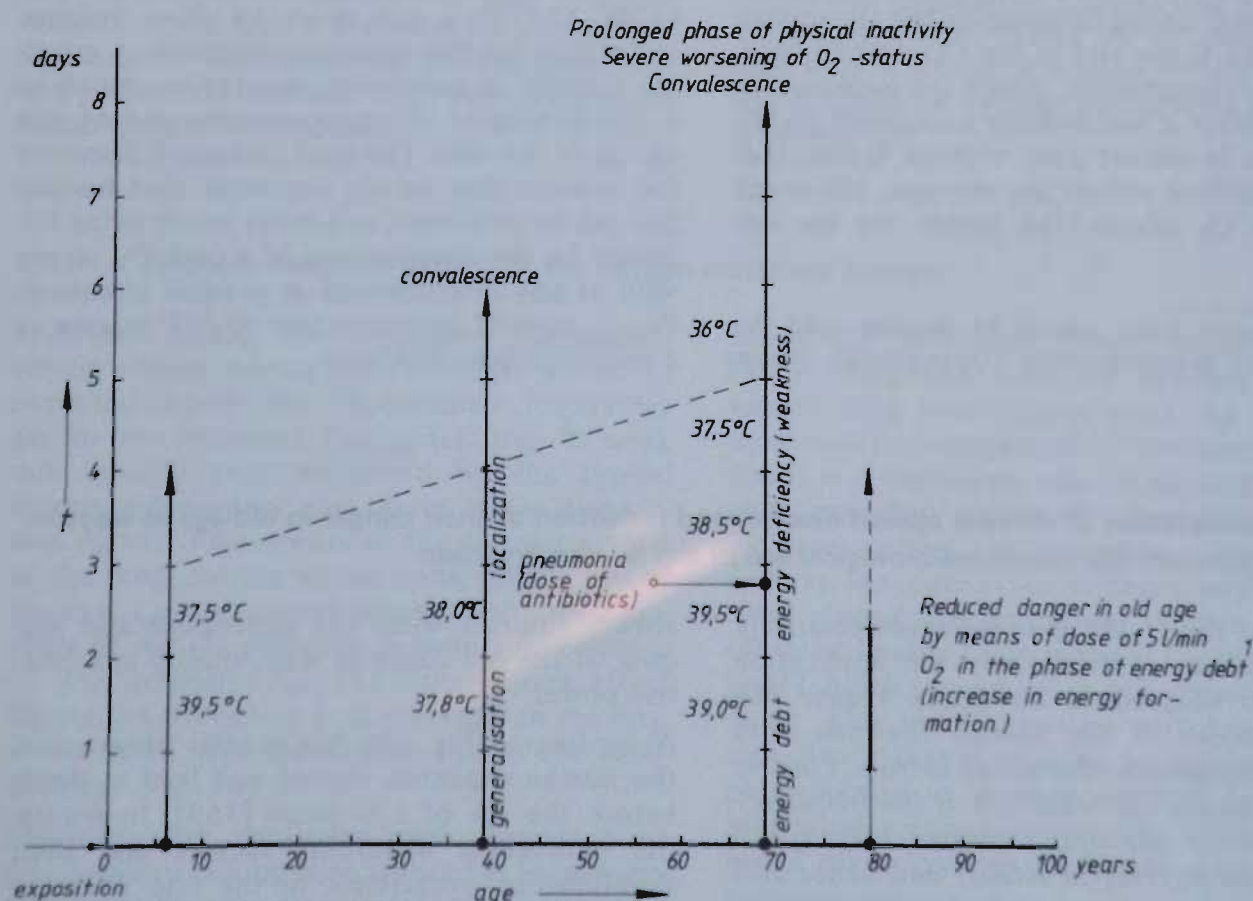


Fig. 237 Effects of the same 'flu' infection in patients of three different age groups. Increase in danger of the infection with age. Reduced danger in old age by application of 5 l/min O_2 in the fever phase (phase of energy debt). Use through O_2 MT technology in own home or through centers with motorized O_2 MT set-ups

¹ Contributions of the O_2 MT procedure variant GK 4-I

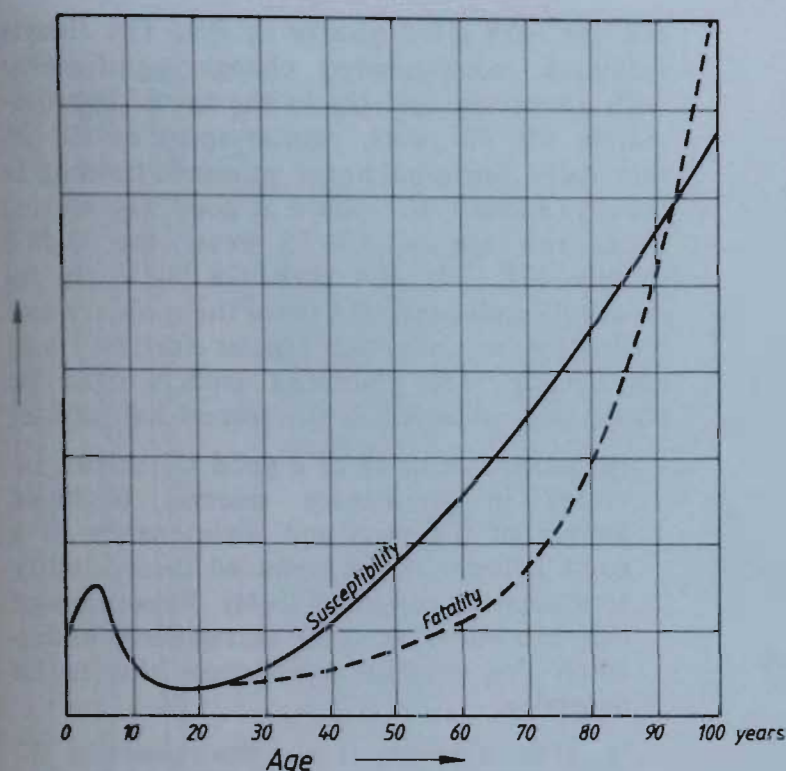


Fig. 238 Susceptibility to and fatality of illnesses, dependent on age, in an arbitrary scale. Normal individuals, no O_2 MT immunostimulation

the gerontologist Simms in New York [370], who concludes from his investigations that "90% of all deaths are predominantly conditioned by the *advanced loss of resistance to illnesses with advanced age*." In [371] the author recognizes and explains with O_2 measurements the fact, closely interwoven with the problem of life expectancy, that the *danger of the illnesses also increases greatly in advanced age*. Figure 237 gives an example of this.

The above recognitions make the analysis and causal combat of the reasons for the increase in susceptibility to, and in the danger of, diseases with advanced age, presented qualitatively in Fig. 238, appear to be one of the major tasks of geriatrics research today.

It is becoming ever clearer from the advances in immunobiology that energy-requiring processes are at work in both non-specific and specific immune defense. It is therefore to be expected that the potency of the body's defense system drops continuously when the energetic status of the human organism deteriorates with advancing age as a result of the drop in the O_2 status.

At least one more contribution with synergistic effect can be added to that discussed above. It results from the *critical decline in the provision of the body's defense substances*. Figure 239 gives an example of how the known reduction in the size of the thymus gland with advancing age affects the correlating decline in thymus factors in the body [372]. It should be remem-

bered that the thymus gland plays a key role as the controlling organ of the immune system, by direct and indirect influence. It follows from the close connection between thymus and immunity that immune deficiency and low resistance are partially due to a lack of immunomodulating substances such as effector substances of the thymus.

The main reasons for the *greater susceptibility to disease in old age* should be sufficiently clear from these explanations.

It is a truism that illnesses lead to conditions of weakness which force the patient to minimize his energy consumption by bed-rest. The extent of the risk grows with the reduction in the energetic reserves for vital organic functions (e.g. detoxification processes in the liver and kidneys). It has already been shown above that old age (cf. Fig. 66) and severe stressful influences (cf. Fig. 60), among them illnesses, cause a deterioration of the O_2 status.

Life-endangering moments occur more and more frequently with advancing age, namely when, with an already reduced O_2 status, further O_2 minima caused by illness, stress etc. occur at the same time as an O_2 minimum in the 24 h day, and thus intensify it (cf. Fig. 10). The results of O_2 measurements and observations shown in this book should make the *occurring deterioration of the O_2 status clearly recognizable as the main cause for the increase in the danger of illnesses with advancing age*.

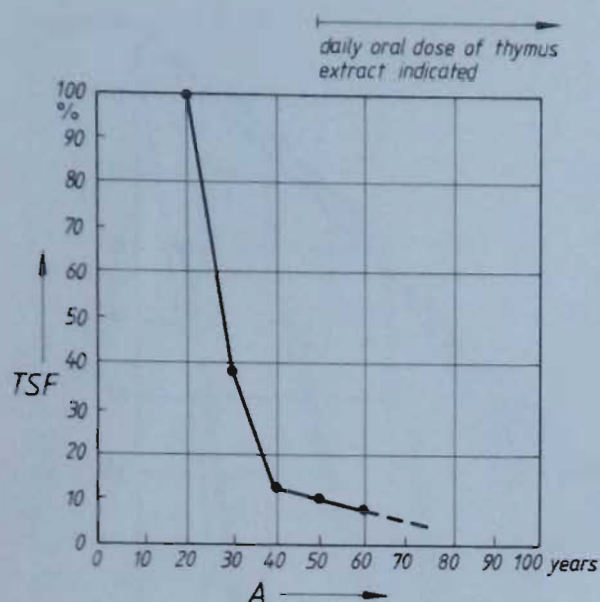


Fig. 239 Thymus serum factor TSF dependent on age A (according to Astaldi 1975)

For the first time in the history of medicine there is the prospect, founded on measurements with statistical significance, of securing *even for very old people a good O₂ status* lasting for many months and even, with regular repetition of the procedure at reasonable intervals, *permanently*. At the same time this effectively combats the hitherto fatal increase in susceptibility to, and in the danger of, diseases in old age. The processes with this effect are the variant GK 2-II, the 15 min O₂MI, and the variant GK 4-IV, the 36 h (18 day) O₂MI, discussed in detail in Paragraphs 4.2.2 and 4.2.4, respectively.

Looking back at the discussed combinations of measures to reduce the susceptibility to, and the danger of, disease in old age, a common principle becomes clear, i.e. the simultaneous energetic and hormonal strengthening of the natural healing powers of the human organism. The body is strengthened to a degree hardly thought possible before, thus corresponding to Hufeland's (1762–1836) old recommendation to strengthen the organism as a means of *combating health crises*.

Figure 240 summarizes the *measures to improve the prospects for the attainment of an*

old age with good quality of life. The fitness measures recommended change significantly with advancing age. Up to the age of approximately 40–45 years, regular sport or 10–15 min daily cardiopulmonary minimal training is usually enough to ensure a good O₂ status. From the age of 40–55 years the O₂MT variants GK 2-II and then GK 4-IV are increasingly indicated, the more the mobility and inclination to undertake regular exercise training decline. The following aspects must be particularly observed in the second half of life:

- Permanent securing of a good O₂ status, increase in circulatory reserves (reduced danger of illnesses) and maintenance of a good defense status (reduced susceptibility to illness) by means of O₂MI. Repetition of this procedure as soon as regularly undertaken PO₂ measurements show this to be necessary.
- In very old age, from approximately 90 years, regular additional implementation of the O₂MT long-term aid, variant GK 6, with an O₂ flow of 2.5 l/min during night-time sleep (O₂ provision from an O₂ Selector whenever possible), one Oxygenabund and one thymus Uvocal dragee at bedtime.
- 10–30 min exercise daily, so far as this is possible (division into 3 daily units if necessary). Exercise training in this late phase of life extends life expectancy.
- Due to stressful influences, e.g. infections, lack of movement, or diseases, the O₂ status drops to the greatly reduced level expected for this age. This means a transition to a life-endangering O₂-deficient condition. It is then of vital importance that no time is wasted in raising the O₂ status to a high level again using O₂MT variants adapted to the patient's condition (cf. also Fig. 237).

For further measures favoring the attainment of a very old age, see [373]; energetic lifestyle, geriatric therapy, nutrition, gerohygiene.

To what extent it is possible to increase further the average life expectancy in populations with highly developed health services, above that of Fig. 241, using the methods described here and with other methods with the same goal, remains to be seen.

5.1.5 Duration of the effect of therapy

The introduction of the special term “*oxygen multistep therapy*” is justified by the fact that a regeneration procedure of relatively short dura-

tion was unexpectedly discovered, which can significantly improve the O₂ uptake of the body and hence the energetic status for weeks,

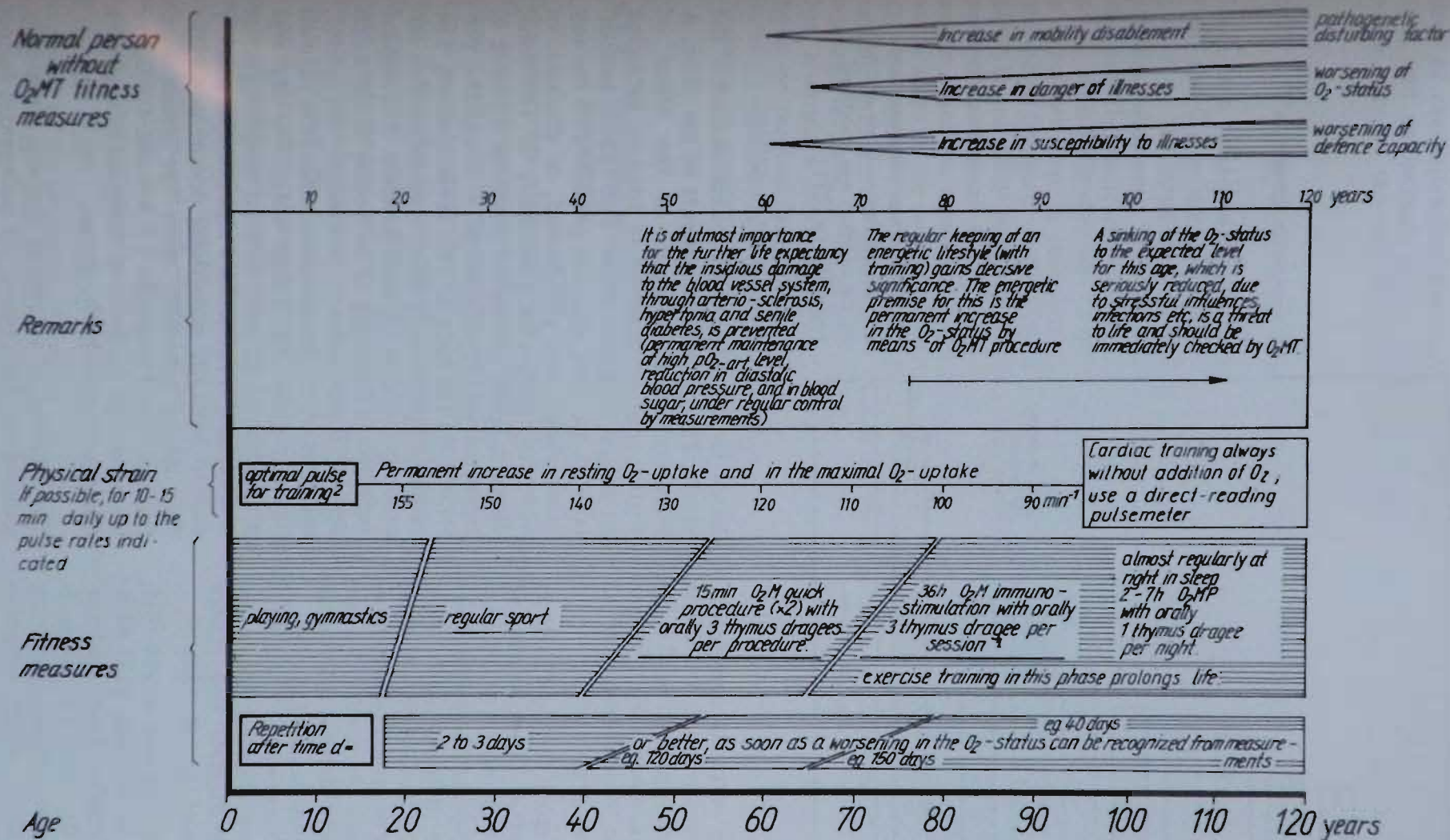


Fig. 240 Ways of bringing individual life expectancy close to the maximum biological age

¹ Simplified non-invasive variant of the procedure of "oxygen multistep immunostimulation" with swallowing of thymus extract on an empty stomach: Thymus Mulli dragees (240 mg dried extract from calf thymus), Fa. Dr. Kurt Mulli Nachf., Otto-Hahn-Str. 2, D-7844 Neuenburg. We had found in WBC counts that the thymus preparation given i.m. versus the oral form is roughly equally effective. Permanent daily dose of one dragee Thym Uvocal[®], also before and after the O_2MT procedures. This program can also be seen as a kind of cancer prophylaxis

² With a simple hometrainer, with the Trimilin rebounding device or with step-climbing method acc. to M. Kaltenbach (cf. Fig. 154). See also Fig. 22, elderly, physically active person: $f = 180$ -age (training rule acc. to W. Hollmann)

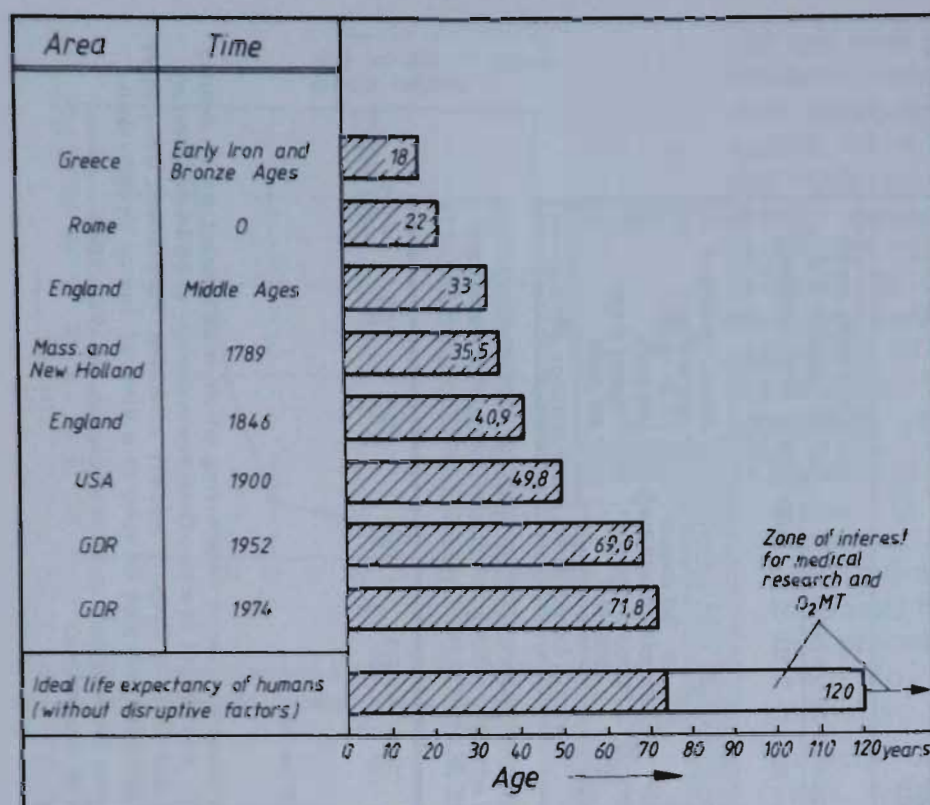


Fig. 241 Mean life expectancy of the population from antiquity to the modern age, modified according to [371]

months and even years after its completion. The term "multistep" was chosen to distinguish this therapy from the usual application of O_2 in medicine, because the combination of several synergetic steps is the characteristic of all variants of the O_2MT basic procedure.

Patients who have undergone the O_2MT rightly ask how long the effect of therapy lasts and when the therapy should be repeated. Patients often spontaneously registered themselves for a repetition because they subjectively felt the fading of the therapeutic effect. A repetition of the procedure is always necessary when stressful influences have caused the level of O_2 uptake of the body to sink again considerably (recognizable from measurements of the PO_{2-art} and PO_{2-ven} at rest, for example). The timing to a meaningful repetition of therapy therefore depends largely on the lifestyle and chance stressful events in the life of the individual.

It has now been proved beyond doubt that, with an energetic lifestyle (cf. Fig. 153) without stress, the effect of therapy (increased product of $\eta \cdot COP$) can last for years. The measurement of the PO_{2-art} at rest, is generally enough to assess the maintenance or critical reduction of the O_2MT effect (cf. Figs 7 and 41) because, as has already been pointed out, the change in the resting PO_{2-ven} is reflected in the dynamics of the PO_{2-art} (same mechanism in the capillaries of the lung and of the other tissue). Caspers [94] proved that the O_2MT effect

lasted for 18 months, by measurements of the resting PO_{2-art} of 108 patients at his clinic. A relatively short duration of the effect of therapy can be observed in patients subjected to critical long-term stress. This applies particularly to patients who are paralysed or for any other reason not able-bodied, or disabled. In order to reduce the probability of additional diseases, O_2MT should be regularly repeated in these patients at intervals of 1–2 months, preferably on the basis of PO_2 measurements. The careful observance of this recommendation can prolong the lives of such patients. The regular repetition of therapy is of course made much simpler if the patient, advised by his doctor, uses one of the less strenuous variants in his own home (e.g. GK 4-1, 5-night cure). For the large proportion of patients without long-term stress it is advisable to consider a repetition of therapy and to have the supervising doctor undertake PO_2 checks whenever there are stressful influences (see Paragraphs 1.1.8.3 and 1.1.9.3 or whenever an increase in complaints suggest a deterioration in the O_2 status.

The chances of successful therapy are greatly reduced in cases where the pathogenic factors have already been irreversibly fixed (e.g. definite vessel wall degeneration of arteries and arterioles, far advanced senile emphysema and other advanced lung diseases with loss of lung parenchyma). In such cases the bioenergetic control of the capillary wall switching mecha-

nism of the microcirculation no longer functions and an increase in O_2 uptake then depends only on the improvement in the steady

state. In such situations (fixed disease) the patient must turn to permanent or long-term procedures (GK 6, O_2 MT long-term aid).

5.1.6 Pathogenic consequences of oxygen deficiency and individual narrowings

Under the collective term " O_2 -deficient conditions and O_2 deficiency diseases", in [2, 159] a survey of the conditions and diseases, whose primary cause must be seen in a long-lasting or chronic O_2 deficiency (energy deficit), was given. Which disorder out of the large spectrum is expressed first in each case depends on the individual situation of the organism and on the lifestyle and other peripheral conditions of the *pathophysiological bottleneck*. Thus, for example, random structural peculiarities in the vasculature in the organism can decide whether O_2 deficiency first leads to weakened sense organs, attacks of angina pectoris or cardio-sclerosis resulting in cardiac infarction, or cerebral sclerosis with consecutive vascular thrombosis or cerebral hemorrhage, or whether circulatory disorders of the extremities first set in, resulting in gangrene, or whether the status of

the host's defense system is so reduced that unrestricted growth of a malignancy begins [376]. It is not unusual for the localization of the deficiency in the organism to make itself felt early by subjective complaints. The observation of such *warning signals* should be seen as cause to begin prophylactic or therapeutic measures immediately. If the cardiopulmonary performance has dropped greatly, the number of sites of deficiency in the organism increases, and the phase of polyathias and multimorbidity (cf. Fig. 236) begins toward the end of life. Conversely it follows from the great variety of pathological consequences of O_2 deficiency that a therapy such as O_2 MT, that lastingly eliminates or alleviates O_2 deficiency, must possess (to an almost disconcerting degree) the characteristic of *great universality*.

5.1.7 Indicated and contraindicated time points for the implementation of the oxygen multistep procedures

The inhalation of gas mixtures with increased O_2 content is normally applied in medicine in phases with poor circulatory condition, with the aim of temporarily supporting the circulation. Examples of this are the utilization of O_2 in emergency situations, in narcosis, in intensive care units and in severe chronic lung insufficiency. In such phases the circulation is particularly affected. The third step of the O_2 MT concept is therefore absent or, more correctly, it is even of a negative character. This is the reason why the procedure with its long-lasting increases in the O_2 uptake and CO_2 production of the organism at rest, unexpectedly discovered in Dresden in 1977/1982, was not found much earlier, e.g. in intensive care units.

For the O_2 MT procedure to be successful (crossing of the switching threshold, lasting increase in the post-procedural value of the product $\eta \cdot COP$, for example) it must, by contrast to the above-mentioned O_2 application, be performed in phases with as good a circulatory condition as possible (selection of timing in daily cycle, increase in cardiac performance by

means of stimulation or support, e.g. g-strophanthin, if necessary).

The treatment is contraindicated at times when spastic processes are occurring in the organism (e.g. attacks with severely increased blood pressure in hypertensives, migraine attacks or perhaps even angina pectoris attacks). Individual observations suggest that the treatment can cause an intensification of the spasms. The administration of spasmolytics may be considered according to the case.

The treatment of epilepsy using O_2 MT is contraindicated because the effect of sedatives is more or less eliminated.

The measurement of the PO_{2-art} at rest and of the η -value should begin from the age of about 50 years, e.g. at intervals of 6 months at first, as a check-up. The O_2 MT procedure should be applied as a preventive measure as soon as the results of PO_2 measurements show levels < 80 mmHg (< 10.6 kPa). This finally results in a *healthy lifestyle with controlled and optimized η or PO_{2-art}* [20, 311].

Table 34 Indications of oxygen multistep therapy. Assembled from objective and subjective findings after several thousand treatments. Examples

Therapeutic aim	Desired effect		Indications	Examples of indications
1. Increase in the energetic status of the whole organism (Combatting falling ill)	1.1	Increased physical and mental strength, also voice power in singers	reduced strength in old age	reduced psycho-physical strength
	1.2	Postponement of multimorbidity in old age	O ₂ deficiency	prolonged phase of high-quality living
	1.3	General risk reduction	certain predictable and non-predictable risks	before plannable operations, during labour, in fever
	1.4	Reduced consequences of stress (especial help in disablement)	results of severe stress	rehabilitation after operations, physical inactivity, heart attacks
	1.5	Intensified benefits of cures and holidays. Improved general well-being	cure, sleeping problems, holiday	prophylactic cures, short holidays
	1.6	Improved defense capacity	weak defense capacity after critical noxae	increased susceptibility to diseases after infections
2. Effects on certain organ systems	2.1 Cardio-vascular effects	2.1.1 Economizing heart work	myocardial ischemia angina pectoris arrhythmia	stenocardia, infarct prophylaxis, rehabilitation after myocardial infarction (check by ECG improvement)
		2.1.2 Normalizing of arterial blood pressure	unfixed essential hypertension regulatorily-conditioned hypertension	symptoms of hypertension; apoplexy (prophylaxis, therapy) Morbus Ménière
		2.1.3 Stabilization of circulation. Reduction in danger of illnesses	general circulation lability circulation lability after specific noxae	dizziness, precollapse; quick rehabilitation after poisoning, burns, radiation
		2.1.4 Renormalizing of O ₂ supply to the arterial vessel walls	arteriosclerosis	signs of first degenerative changes (e.g. ocular fundus)
		2.1.5 Combatting circulatory disorders and their consequences	arterial circulatory disorders in the extremities	pre-gangrene, lower leg edema, "smoker's leg"; walking distance multiplied
	2.2 Lung effects	2.2.1 Amelioration of treatable lung diseases	chronic bronchitis bronchial asthma	clearing of prolonged dizziness and breathing difficulties, asthma attacks less frequent

Table 34 (Continuation)

Therapeutic aim	Desired effect		Indications	Examples of indications	
	2.3 Effects on CNS and sense organs	2.3.1 Increased energy metabolism in brain. Increased ability to concentrate	cerebral sclerosis conditions after apoplexy	loss of memory, confusion; remaining damage after apoplexy	
		2.3.2 Reduced frequency and severity of migraine attacks	migraine reduced reaction times	sleep disturbances (esp. in migraine)	
		2.3.3 Influence on certain ophthalmological diseases	cataract other O ₂ deficiency disorders, retina edema	senile cataract sharp decrease in visual acuity, pathological light sensitivity, field of vision narrowed	
		2.3.4 Influence on certain ENT diseases	decreased hearing, esp. in old age	otosclerosis combatting sudden loss of hearing	
		2.3.5 Deceleration of multiple sclerosis	multiple sclerosis	effects of additional noxae, e.g. 'flu, reduced	
	2.4 Liver and kidney effects	2.4.1 Influence on certain liver diseases	cirrhosis of the liver adiposis hepatica	increased transaminases, e.g. through alcohol abuse	
		2.4.2 Influence on certain kidney diseases	chronic kidney insufficiency	life-long dialysis patients	
	2.5 Influence on certain endocrine diseases		diabetes mellitus	senile diabetes (e.g. reduced use of medicaments)	
	2.6 Improvement of wound healing		burns decubitus	above 20% body surface decubitus prophylaxis	
	3. O ₂ multistep immunostimulation (O ₂ MI)	3.1 Favourable influence on chronic inflammations	3.1.1 Amelioration of rheumatic diseases	primarily chronic poly-arthritis	acute exacerbations
			3.1.2 Amelioration of certain diseases of the joints	degenerative arthropathies	arthroses
		3.2 Favourable influence on malignant neoplasms	3.2.1 Reduced probability of cancer incidence	cancer prophylaxis	general cancer prophylaxis
			3.2.2 Reduced probability of cancer relapses and metastases	cancer relapse and metastasis prophylaxis	post-therapy prophylaxis (operation, radiation, chemotherapy, CMT)
			3.2.3 Amelioration of late symptoms of cancer. Weight gain	tumour cachexia (prolonged phase of high quality of life)	nausea, dizziness, loss of appetite in late stage
		3.3 Combatting falling ill	3.3.1 Reduced susceptibility to disease	increase life expectancy	measure in later life

5.1.8 Indications for oxygen multistep therapy

Table 34, which shows the indications for O_2MT , was compiled from objective and subjective findings before and after several thousand O_2MT treatments in numerous institutes both in the GDR and abroad. The table is subdivided into types of application with different therapeutic aims. Column I shows the variants that mainly serve to *combat falling ill* and whose preventative effect is mainly due to a general increase in the energetic status in the organism. In column II the aim of therapy stretches to the *combat of diseases and complaints already manifest in certain organ systems*. The third column refers to the utilization of *oxygen multistep immunostimulation* (O_2MI), which is

not discussed until the last section of this book. Other special indications are discussed in Paragraphs 4.2.2 (obstetrics procedure) and 4.2.4 and 1.1.7 (combat of placenta insufficiency).

The foundations of the table of indications rest also on numerous case reports containing *interesting successes of the O_2MT and the O_2MT in treatment*. This documentation, which is already the size of a long book, is available to interested medical practitioners for perusal in the Clinical Research Department of our Institute.

The clinically preferable procedural variants of the O_2MT have been presented in Table 23.

5.1.9 Oxygen multistep therapy as a supplement to classical or pharmacological treatment

The leading representatives (officials, superintendents) of the cure spas should more and more recognize and utilize the fact that the combination of their cure measures with the O_2MT signifies a *medically and economically important activation of their facilities*. This is because the O_2MT procedures as a basic therapy intensify almost all the effects of the classical cures very considerably, due to the long-term increase in the energetic and immune status. Examples here are thermal baths, mud-baths, Kneipp baths, special swimming pools, all kinds of massage, fitness training, measures from respiratory physiology, from physiotherapy and dietetics, etc. Measures of this kind, performed under the control of the doctor before the start of O_2MT , can, among other things, reduce restricted movement, improve the prospects for the obligatory more

energetic lifestyle after therapy, and represent preconditioning. The advantages that arise for both classical cures and O_2MT from their combination mean that the *O_2MT should not be regarded as a competitor to classical cures, but as a useful supplement to them* (basic therapy).

A similar situation exists in treatment with drugs. O_2MT must not be generally categorized as a competitor to pharmacological treatment. For many indications the *effect of O_2MT on certain organs or tissues is supplemented by specifically aligned drugs*.

Primarily we should value and exploit the fact that many serious *side-effects of drugs can be alleviated or eliminated by the O_2MT* (strengthening of the detoxifying organs; utilization in psychochemotherapy, cancer chemotherapy etc.).

5.1.10 Documentation of results of therapy

An important feature of the O_2MT is that the situation at the onset and the *success of therapy can be given as numerical values*: PO_{2-art} , PO_{2-ven} , η -value, QO_2 , all determined at rest, PWC, QCO_2 , visual and acoustic reaction time, biological age etc. The measurement of the PO_2 and hence also of the η -value, which is easy to perform routinely, has gained great practical significance. This feature of the O_2MT should, in the interests of both patient and doctor, be utilized in every treatment by the careful *documentation of the results of treatment*. Forms

are available for the documentation; Fig. 242 shows an example. It is also useful to include the *Karnofsky index* in the documentation, as in Table 35. A series of typical case reports have been published in [18]. We normally allow the patient to see the documentation of his case and even make a copy of it available to him. This deepens his comprehension of O_2MT and increases his compliance and his willingness to undergo repetitions of therapy and to switch to a more energetic lifestyle.

O₂ MT institution (address): Dr. med. Hans Müller-Winter
CH-7320 Sargans

Patient (code): AA Age: 54 Sex: male Date: 5.7.1984

Clinical condition before therapy (if relevant, indicate Karnofsky index, BP, etc.)

After cardiac infarction: attacks of angina pectoris even during light physical exertion, also often when resting. ECG: biphasic T-waves V4-V6. Patient can only walk about 100 m without complaints; has been unable to work for several months.
Karnofsky index (KI): 65%

Diagnosis: State after cardiac infarction

Previous therapy:

<u>O₂ status before therapy:</u>	$P_{O_2\text{-art}}$	$P_{O_2\text{-ven}}$	η	$\dot{Q}_{O_2}$
Time of measurement: 9.00 a.m.	70 mmHg	35 mmHg	26%	1 · min ⁻¹

O₂ MT variant: GK 4-I

<u>O₂ status after therapy:</u>	$P_{O_2\text{-art}}$	$P_{O_2\text{-ven}}$	η	$\dot{Q}_{O_2}$
Time of measurement: 9.00 a.m.	80 mmHg	30 mmHg	37%	1 · min ⁻¹

Clinical condition after therapy (if relevant, indicate Karnofsky index, BP, etc.)

(Result of therapy)

Attacks of angina pectoris have disappeared.
ECG: nothing abnormal discovered.
Patient takes part in mountain rambles and is practically free of complaints.
Working again full-time in his career KI: 95%.

Fig. 242 Example of rehabilitation after cardiac infarction. Result of treatment

Table 35 Table of Karnofsky Index

Karnofsky Index	Criteria	Strain capacity
100%	no complaints	able-bodied
90%	slight symptoms of the basic disease normal performance	
80%	fully-developed symptoms of the basic disease normal physical performance only with effort	
70%	self-care, but no physical strain possible	performance limited
60%	partial help needed in self-care	
50%	help usually needed, partly bed-bound	
40%	predominantly bed-bound, hospitalization not necessary	self-care no longer possible
30%	completely bed-bound; no immediate threat to life	
20%	severely ill, hospitalization necessary	
10%	moribund	

5.2 Increase in physical performance capacity and combat of oxygen deficiency conditions

5.2.1 Increase in physical strength. Transition to a more energetic lifestyle

An increase in the physical performance capacity not only occurs after completion of O_2MT but rather, with almost all variants with advancing development of the switching process of the blood microcirculation, there is a continuous increase even during the treatment. This immediate response is of very great significance in the 120–60 min O_2MT obstetrics procedure, GK 2-IV, because our measurements have shown that a performance of 150–200 watts must be attained by the mother during the expulsive stage. The increase is usually approximately 30% (duration of labor shortened, avoidance of non-vaginal deliveries). The increase in physical strength during the O_2 inhalation can be utilized to treat even patients who cannot cope with much exertion with the time-saving but strengthening 15 min O_2MT quick procedure, GK 2-I, under medical supervision. Figures 125 and 224 give examples of this. Figure 89 shows an example in which a great increase in physical performance capacity in an infarct patient can be seen after just approximately 12 h of the 36 h O_2MT procedure, variant GK 4-I.

For the lasting increase in physical performance

capacity after O_2MT the reader should refer to the double-blind study [61] and our spirometric findings [466] which show that a lasting increase of 15% (healthy persons) to 80% (weakened persons) in the CO_2 production at rest can be observed after O_2MT (the CO_2 production is roughly proportional to the formation of energy-rich phosphates). This fascinating results accord well with the ergometric observation in Fig. 24. It is a basic demand of the O_2MT that this gain in physical energy be utilized for the more energetic lifestyle (new formation of muscle). Even the smaller increase in strength in healthy individuals can help singers and actors before major performances, for example, or politicians and managers before particular events. The lasting increase in strength attainable could well determine victory or defeat in sporting competitions. The coach of a football team that undertook two treatments with the O_2MT GK 2-I variant in the Klinik für Naturheilverfahren in Bad Füssing, FRG, (Dr Caspers) a few days before each major match, twice informed the author of victories against far superior opponents and of his players' surprising concentration and freshness in the second half.

5.2.2 Oxygen multistep therapy and erectile dysfunction (impotence)

The author has received several reports of an alleviation of impotence after O_2MT . These observations suggest that it is useful to combine the O_2MT , which considerably increases the physical performance capacity, with the SKAT method [378] developed by Bähren and colleagues (University of Ulm, FRG). With this method an α blocker and papaverine are injected in both cavernous bodies. The α blockers serve to dilate the pelvic arteries in order to increase circulation there. Papaverine facilitates the unhindered influx of blood into the penis by relaxing the musculature in the walls in the cavernous bodies. The erection lasts, according to findings by Wehnert (Urological Clinic, Medical Academy of Dresden, GDR), approximately 60–120 min. The practical process, cf. [378], is as follows: the injection solution is made up of 30 mg papaverin hydrochloride and 1 mg phentolamine methane sulfonate (Regitin, from Ciba-Geigy, Basle, Switzerland) in 2 ml sterile physiological saline

The corpus cavernosum is punctured right and left laterally from the dorsal middle of the root of the penis, vertically at a depth of 10 (to 5) mm using a disposable needle 0.45·13 mm (Sterican G·1/2") under sterile conditions (disinfectant spray). The dosage varies between 0.05 and 3.0 ml of the given solution, depending on the extent of the erectile disorder. Prolonged erection over several hours can occur as a relevant side-effect (antidote). The age-limit of the Ulm autotherapy, which until now has ended at approximately 60 years, is increased by 20–25 years by combination with O_2MT (significant increase in physical performance capacity).

A new vibrating injection syringe, developed by Roggenbuck and the author for this purposes, can be of help in this problem. This syringe has the following features: an electrically driven motor vibrator sets the fine cannula of a disposable syringe into axial swinging motions, so

the cannula enters the required depth of the tissue (10 or 5 mm) virtually painlessly. First the front plate of the injection unit is placed on the selected tissue surface. Then the small motor drive pushes the vibrating needle through an opening in the front plate to a stop that determines the depth of the injection, and finally the same drive pushes the plunger of the 2 ml disposable syringe forward. The total time required for this is about 15 s. This new type of syringe with its low pain function should prove to be useful in several branches of medicine. A *special double syringe* with this operational method (GDR patent pending) adapted to the above task has also been developed. It has two axially vibrating needles, separated by 14 or 11 or 7.5 mm, which are fed via a T-tube from a 2 ml syringe. The needles, tube and syringe are all disposable. After the cylindrically shaped front part has been placed from above on the dorsal corpus cavernosum tissue

and a small switch has been operated, the double injection process with its discussed functions runs fully automatically.

In the following detailed discussion of fields of operation of the O_2MT , the reader should recall the reservations expressed in the preface. We only have experience with larger numbers of patients with a few, albeit important types of application. With other types of application the positive results of a small number of individual experiments only justify hopes. With a further group of types of application we do not as yet have any practical experience. Nevertheless, we should not fail, in the framework of this book, to recommend that they be tried, because positive effects are to be expected in accordance with the underlying physiological processes. The relevant paragraphs therefore signify nothing more than an encouragement of medical researchers of the disciplines concerned to be active.

5.2.3 Arteriosclerosis

As regards morbidity and mortality, *arteriosclerosis with its secondary diseases* (angina pectoris, myocardiac infarction, stroke etc.) *stands at the head of all diseases in modern industrial states* [380]. Combat of it is one of the most important medical problems of our time. The reason why we discuss arteriosclerosis here is that it also decisively contributes to the genesis of most of the other O_2 deficiency conditions and diseases discussed. The tumescence of the arterial vessel wall cells, characteristic of early arteriosclerotic changes and the relevant noxae, have been discussed in Paragraph 1.1.1. It is claimed, not unjustifiably, that the human is as old as the condition of his vascular system, and the topography of this condition determines how well or how poorly the individual organs of the organism are perfused with blood and supplied with oxygen (energy).

The *prophylactic combat of arteriosclerosis* is one of the main tasks of preventive medicine, for it shows no symptoms in its early phases and when pathologic signs are recognized in its advanced stage, it is usually too late for therapy because the changes are irreversible.

Arteriosclerosis is an O_2 deficiency disease in which the drop in the PO_{2-art} (e.g. hitherto age-conditioned) leads directly to a weakening of the O_2 metabolism in the endangered tissue area (walls and ramification points of the arterial blood vessels), and in which, therefore, no "protection" is afforded by the saturation

character of the upper part of the HbO_2 dissociation curve (cf. Fig. 124 above). Conversely, the same reasons lead us to expect particularly positive prophylactic effects if the PO_{2-art} , at rest, is kept at high levels over many years by regular, strength-requiring exercise training (e.g. certain sports, mountain inhabitants, home trainers), or if an already considerably reduced PO_{2-art} is permanently raised again to levels that existed in the best years of youth, by means of several variants of the O_2MT (see Paragraph 4.).

The methodological basis of this kind of *prophylaxis* of arteriosclerosis is the numerical calculation of the PO_2 in the interior of the arterial vessel walls, according to the *two-dimensional diffusion equation* shown in Fig. 243. The calculation showed that the O_2 supply to the middle of the vessel wall by diffusion from the lumen reaches critically low levels when the resting PO_{2-art} drops below 75–80 mmHg (10–10.7 kPa). This resulted in the idea that the sclerotic degeneration of the arterial vessel walls can be the better delayed, the better the PO_{2-art} can be kept by O_2MT with as few interruptions as possible at levels above 75–80 mmHg from an age of about 50–60 years. The O_2MT concept is still young, and the timespan for the observation of prophylactic effects is certainly decades in the case of arteriosclerosis. The only volunteer who has lived over approximately 15 years (from the age of 65 to 81) almost uninter-

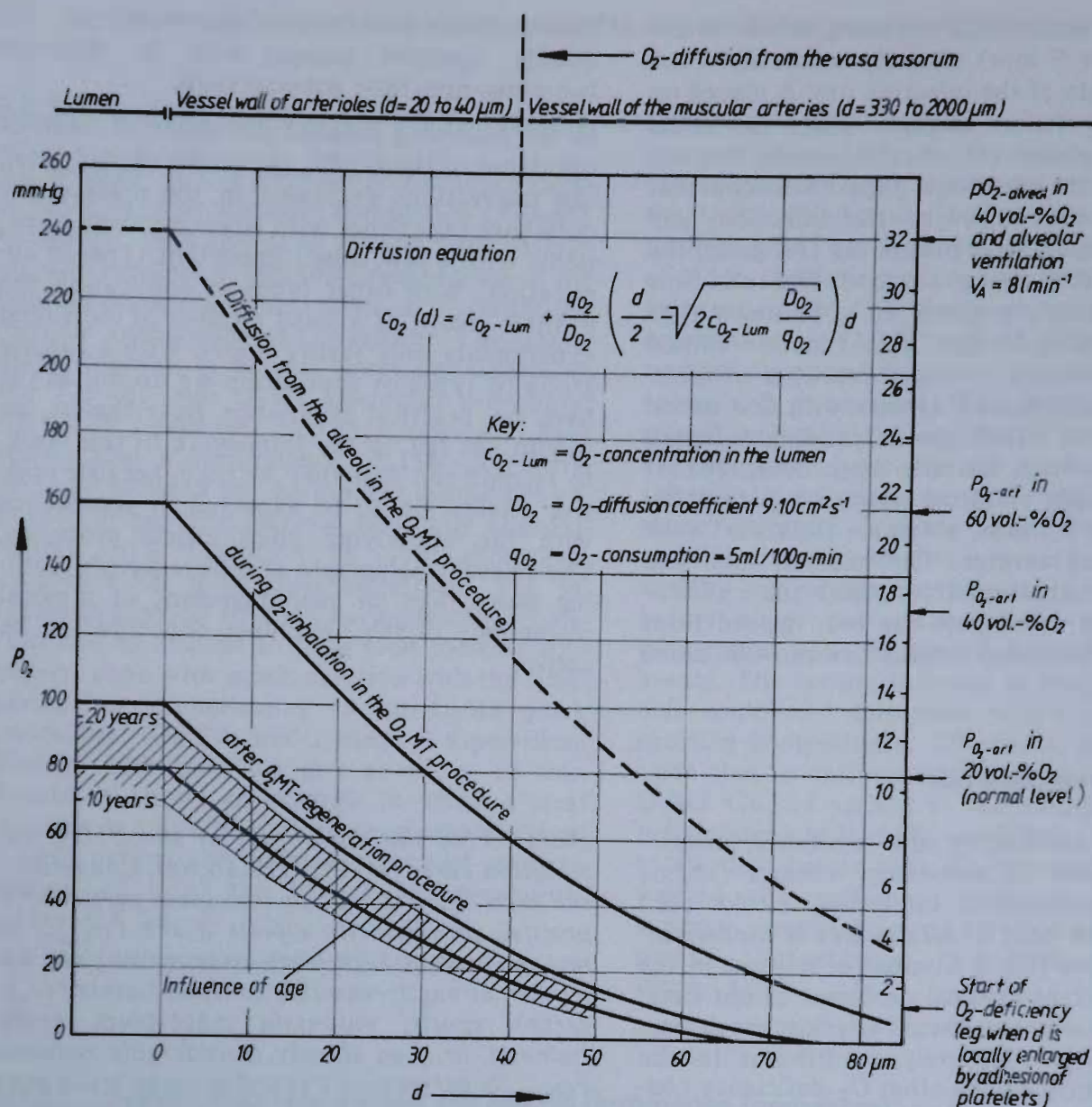


Fig. 243 Quantitative presentation of the very great increase in the PO_2 produced in the lumen of the arterial vessel wall, by means of increase in the O_2 proportion in the inhalation air from 20 vol.-% (normal level) to 40 or 60 vol.-%. A. and M. von Ardenne 1977, unpublished. Result: O_2 deficiency favored in a priori thickened arterial wall areas or those narrowed by clinging blood constituents. Conclusion: maintenance of $PO_{2-arteri}$ levels, measured at rest, around or above 80 mmHg (10.6 kPa) for decades

ruptedly with levels of the $PO_{2-arteri}$, at rest, above 80 mmHg (10.7 kPa), is the author. Perhaps the measurement in Fig. 212 A (see Paragraph 3.4.4), which allows us to conclude that his vascular system is in an extraordinarily good condition, is a first indication of the success of arteriosclerosis prophylaxis by the utilization of the O_2 MT over decades. The following finding indicates that this assessment is very probably true: it was possible to normalize the blood pressure to a considerable extent in almost all hypertensive patients with not yet chronic high values, by means of the high-charging of the O_2 status (especially of the

$PO_{2-arteri}$) with few interruptions over many years, using the O_2 MT variants GK 4-I or GK 2-I. Blood pressure reducing substances were given adjuvantly in strongly reduced doses.

By arteriosclerosis we understand a disease of the arteries which involves changes, particularly thickening and finally hardening, in the vessel wall. The disease begins insidiously (cf. Fig. 236), the pathological process not being accompanied by pain or typical symptoms. It is not usually until the late stage, when the defective texture of the vessel wall layers is irreversibly established, especially at the ramifications, that

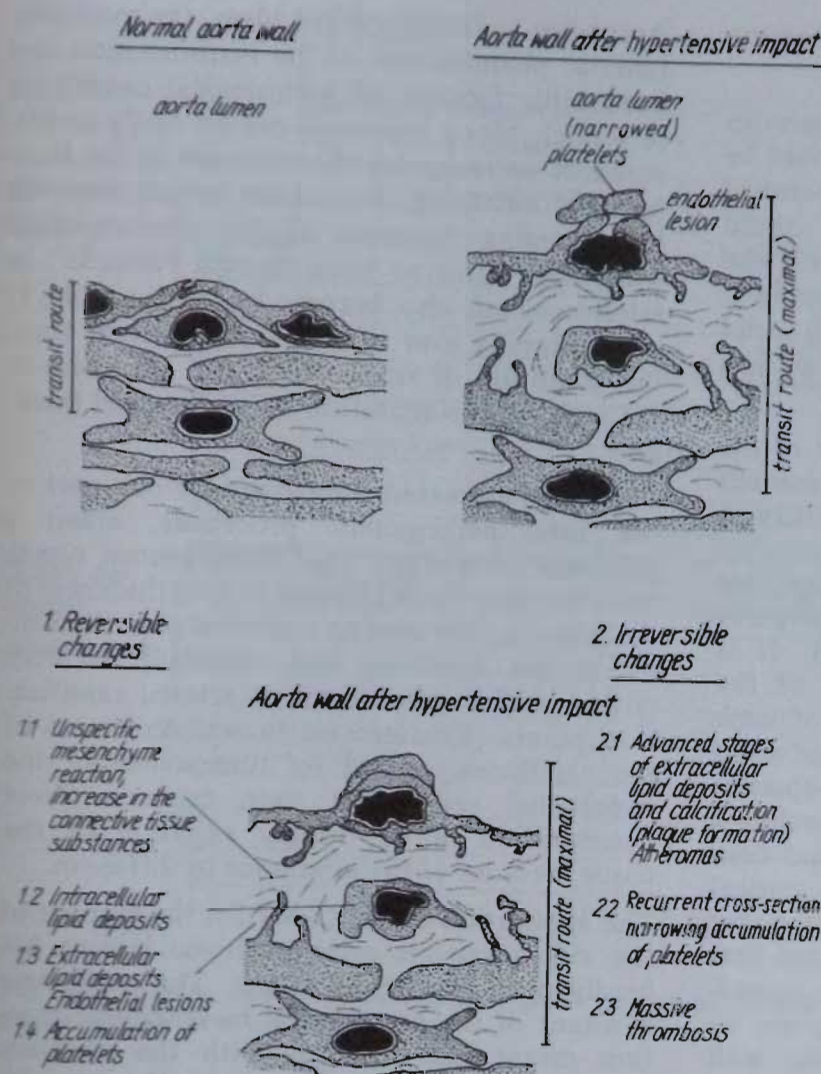


Fig. 244 Schematic presentation of reversible and irreversible arteriosclerotic changes in the aorta wall. Modified after Hauss, Ross-Harker

a severe constriction or occlusion of the arterial lumen leads to often fatal complications, such as myocardial infarction and stroke. The last decade has produced new thoughts and findings in arteriosclerosis research, mainly by the work of Hauss and his school, which were presented in Paragraph 1.4.7 and which will be dealt with again further below. By radiolabelling, and with the aid of electronmicroscopy, Hauss gains morphological ideas that are presented in Fig. 244. Sclerogenous noxae (cf. Table 11), to which O_2 deficiency also belongs, can lead to a massive incorporation of mesenchyme into the vessel wall within 30–60 min (cf. Fig. 113). At the same time there occur lesions of the endothelium, which result in the lumen-constricting attachment and aggregation of platelets there [383]. Both these processes cause a significant local extension of the transition zone through which the intima and media of the arterial vessel wall are nourished, mainly by diffusion from the lumen. The increased wall thickness also means that the priming O_2 deficit additionally intensifies the O_2 deficiency in the center of the vessel wall, due to the extension of the

diffusion length (feedback). This also explains the intermittent [193] and also localized appearance of the arteriosclerosis.

Various observations of our own have led us to the view that the critical wall thickening maintains its reversible character for long periods of time (Fig. 244 below) and that the best way to bring about the "favorable" condition for the labile vessel wall system (feedback, flip-flop mechanism), lies in the reversal of the sclerogenous noxa named O_2 deficiency. A practical method of achieving this is the very great increase in the PO_{2-art} during the O_2MT procedure (cf. Fig. 7) and the resulting extreme, temporary increase in the oxidative metabolism in the arterial vessel walls, combined with the permanent raising of the PO_{2-art} , under resting conditions, discussed in Paragraph 1.1.8.4.

In connection with this we include a working hypothesis that led the author to the O_2MT in 1970: the intensification of the O_2 metabolism signifies an increase in the energetic status. The aim is to purify the arterial vascular system. Purification is always a process requir-

ing much energy. Thus the way to purification is the raising of the energetic status.

Just as false nutrition is one of the sclerogenous noxae (cf. Table 11), a suitable diet should be an "anti-noxa". From the quantitative point of view, however, the variants of the O₂MT should trigger much stronger effects than, say, the recently more discussed dietetic measures (e.g. with polyunsaturated fatty acids). Only strict fasting is an exception here, and we will go into more detail on this subject below.

The *irreversible vessel wall degeneration of the arteries*, which lead to hardening, permanent cross-section narrowings, a loss of elasticity in the wall, fragility and thromboses, occur, according to established medical knowledge, due to the gradual deposition of hard-to-degrade substances (cholesterol, calcium salts). It is plausible to assume that the amount of the deposits correlates with the amount of time over which a severe thickening of the vessel wall has existed as a result of the non-specific mesenchyme reaction (excessive mesenchyme metabolism). According to the discussed concept of the flip-flop mechanism, the critical arterial wall areas should by preference either be weak or thickened. The combat of the irreversible arteriosclerotic lesions aims, in accordance with what has been said, to keep the influence of factors that favor vascular wall thickenings as short as possible. This means that the application of the O₂MT as a prophylactic measure should be begun early enough, as has already been emphasized above, i.e. at times when the O₂ deficient intervals that cause a thickening of the vessel wall are still rare. A good timepoint to begin this prophylaxis would be between the ages 50 and 60, or, in persons with a special disposition, between the ages of 40 and 45 years (cf. Fig. 123). Strict fasting should also be mentioned here as a synergistic method, in which strong lipolysis in the arterial vessel walls should cause deposited lipids (Fig. 244) to be partially broken down. The supplementation of the O₂MT measures by means of drugs to influence the critical mechanism of thrombocyte deposition and aggregation must also be investigated.

5.2.4 Regulatorily conditioned hypotension

Part of the price that the human must pay for turning away from the natural, physically active way of life is the *increased frequency of regulatorily conditioned hypotonia*. The performance capacity, health and life of the human

According to the developed ideas, the medically familiar phenomenon of the manifestation and irreversible fixation of pathological conditions (e.g. high blood pressure) can be easily understood. If we recognize the existence of the feedback or switching mechanism which controls the changing thickness of the arteries, then what have hitherto been termed "attacks" in arteriosclerosis also become understandable. It is the tipping over of a bi-stable system from the condition of small vessel wall thickness to the unfavorable condition of great vessel thickness.

The ideas presented only consider one part of the total pathogenetic procedure, albeit a particular important one. Sclerogenous noxae not only lead to an increase in wall thickness in the arteries, but also to a certain wall thickening in the arterioles and, especially, to very critical wall degenerations at arterial ramification points. The increase in wall thickness of the capillaries, caused by tumescence of the endothelial cells must even cause a direct deterioration in the supply situation of the tissue, because of the hindrance of diffusion.

The application of the O₂MT for the combat of the still reversible arteriosclerotic lesions has hardly been researched as yet. The small time constant of the non-specific mesenchyme reaction means that here, as with the capillary endothelial cell reaction, *instant effects* can be observed or expected after completion of the treatment. The O₂MT effects against hypotension and hypertension, discussed in the next paragraphs, must be categorized as instant effects of this type. However, the presented views as to the mechanism of the therapeutic action in the critical areas of the arterial walls still require a more deliberate adaption to directions of modern arteriosclerosis research, which could only be mentioned here [e.g., 383, 384]. This offers the researching and practising doctor an occupational field of great topicality. For such work we refer the reader to the GK 2-I, GK 4-I, GK 4-II, GK 7 variants and also to the KA 1 variant, whose application is discussed separately in the following paragraph.

are more and more frequently threatened by too low blood pressure levels with too small blood pressure amplitude, and a low PO_{2-art} , or the circulatory disorders connected with it. Until now no means have been known lastingly

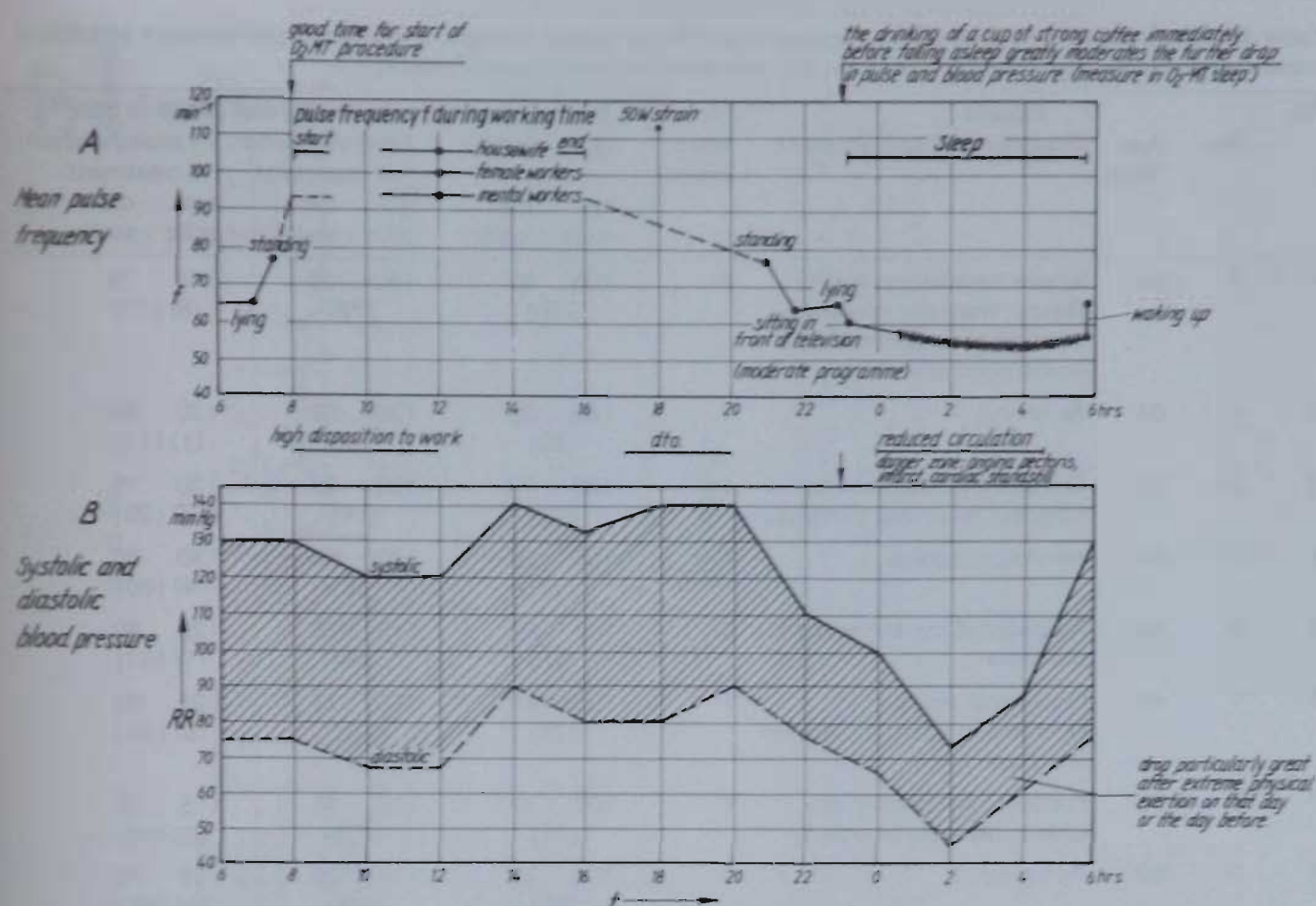


Fig. 245 Guiding values for the course of pulse frequency (A) and blood pressure (B) of healthy subjects during the 24 h cycle of a working day

to eliminate this critical condition. Only recently have temporary successes with the combination preparation *Ergomimet plus* (dihydroergotamine + etilefrin) been reported [359]. The 80 min O_2MT nicotinic acid procedure for the head and neck area (variant KA 1, Table 32, Paragraph 4.3.1) can often give decisive aid here, for a single or double application of it eliminates the regulatorily conditioned hypotension over months or years in very many cases (success rate > 50%) [106, 360].

The procedure should only be applied under medical supervision because of the strain on the heart and circulation connected with it. In addition, nicotinic acid can (albeit very rarely) trigger allergic reactions (release of histamin) which demand administration of antihistamines. A perlingual administration of 6 mg g-strophanthin from a high concentrate (Strodival special capsule) is included, to support the heart and the therapeutic procedure.

In practical work the question of the best time of day for the O_2MT KA 1 variant arises. The best time is when there is particularly good

circulation of the tissue and also particularly high performance capacity, i.e. at about 10.00 a.m. On this, and to supplement Paragraph 5.1.7, Fig. 245 shows guiding levels as to the course of the pulse rate and blood pressure of a healthy person (age $\approx$ 45 years) during the 24 h cycle of a working day. This presentation also explains why it is recommended to drink a cup of strong coffee at bedtime in suitable cases for the O_2MT sleep.

Examples of the therapeutic effect of the KA 1 procedure (cf. Table 32) in hypertensives from the year 1971 are summarized in Table 36. Since then this procedure has been applied in more than one hundred patients, with similar results. Only those patients were treated who through medical examination, including an electrocardiogram, showed to be suffering from hypotension which was not caused by organic cardiac diseases.

The blood pressure was measured using the conventional noninvasive Riva-Rocci method, which is to be regarded as accurate enough for the detection of the occurring blood pressure

Table 36 Measurements on several hypotensives to show the lasting increase of systolic blood pressure and blood pressure amplitude after treatment with the O₂ multistep procedure as in Table 32

No.	Sex	Age Years	Patient Diagnosis before treatment	No. of treat- ments	RR blood pressure in mmHg and [pulse in min ⁻¹]					
					before treat- ment		1 day after end of treatment		() months after treatment	
					sys- tolic	dia- stolic	sys- tolic	dia- stolic	sys- tolic	dia- stolic
1	♂	64	Severe circulatory insufficiency; frequent triggering of crises after sclerogenous noxae (strains)	4	105 [70]	80	150 [72]	75	140 (8)	75 [72]
2	♂	64	As for no. 1	1	105 [70]	80	120 [69]	80	120 (1)	80 [72]
3	♀	51	Circulatory insufficiency; frequent dizziness, tiredness	1	100 [75]	75	120 [74]	80	120 (12)	75 [76]
4	♀	60	Vertigo; tiredness	1	105 [76]	80	120 [76]	80	130 (14)	80 [80]
5	♂	48	Frequent dizziness: vertigo, tiredness	1	100 [65]	60	115 [68]	75	125 (1)	80 [67]
6	♀	43	Occasional vertigo Decrease in vitality, frequent tiredness	1	105 [74]	80	115 [76]	75	125 (8)	80 [76]
7	♂	55	Frequent circulatory disorders, decrease in vitality	1	100 [71]	70	115 [71]	70	115 (6)	75 [68]
8	♀	62	As for no. 1	1	100 [66]	75	115 [65]	75	115 (1)	75 [66]

changes. The pulse was always measured simultaneously with the RR values. The measurements were taken "at rest" in the mornings in patients with an empty stomach, without exertion, in a sitting position after a rest of approximately 10 min. The first, undisturbed (usually lowest) measured value was recorded. Most measurements were done in triplicate at 5 minute intervals, with calculation of the arithmetic mean and rounding-off of the result.

As has already been mentioned, the hypertensive drugs available today increase the blood pressure and its amplitude only temporarily and slightly (up to 6–8 h using depot preparations). By contrast, a strong effect lasting over *many months even to many years* was observed in nearly all trials with the KA 1 variant. Because of the changes in blood pressure during treatment it is recommended that the first measurement to assess the result of the procedure be undertaken one day afterwards, with further measurement in the course of a few weeks or months. In studies including only individuals with noncardially conditioned hypotension, there was normally *an increase in blood pressure amplitude of between 5 and 15 mmHg*

(0.66–2 kPa), on the day after the treatment. Observations over some years have ascertained that, in several cases, the blood pressure amplitude, raised by the therapy, dropped again if the patient was subject to the noxae discussed above, for longer periods of time.

The result of a single experiment, undertaken as a spot check on an older person with normal blood pressure, showed that, here too, the blood pressure amplitude rose and remained high, namely 160/80 mmHg (21.3/10.6 kPa) in the first two days after treatment. The outcome of this single experiment compels us to warn against the application of the KA 1 variant in hypertensives in the later stage.

Repetitions of the therapy procedure can increase the systolic blood pressure and the blood pressure amplitude in stages, as the example in Fig. 246 shows. Here the blood pressure amplitude of a hypotensive patient was increased from 25 to finally 60 mmHg, and was maintained for more than 15 years. In all trials performed so far, the patient's circulatory stability and his stress and performance capacity were significantly increased, correlating with the increased blood pressure brought about. Despite

Alteration of the mean blood pressure amplitude from: 25 to 40

40 to 55

9 months later!
60 mmHg

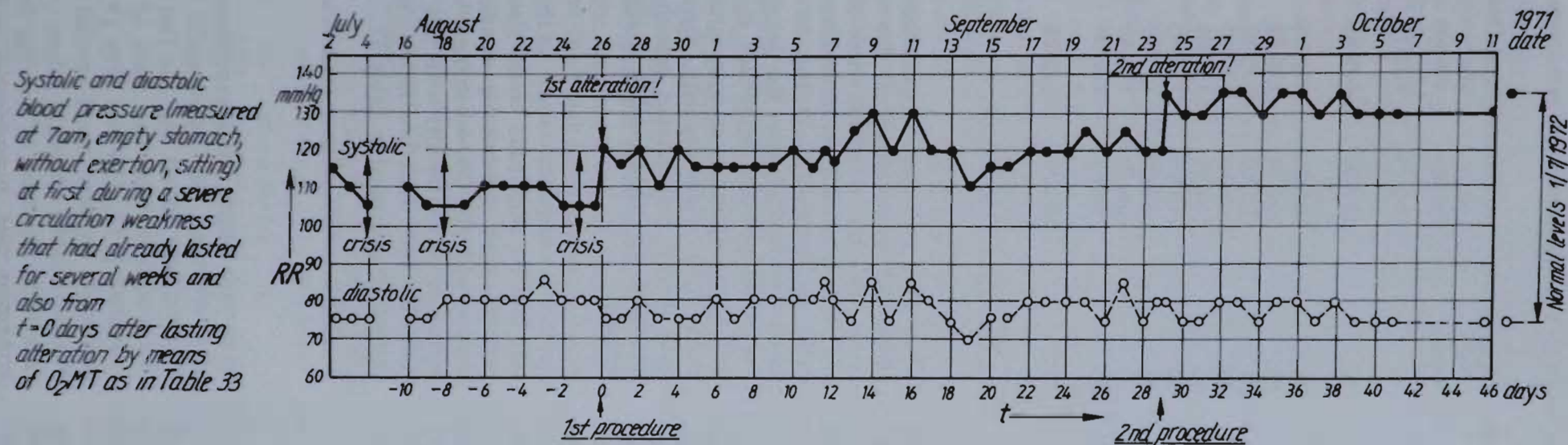


Fig. 246 Measurements of the lasting increase in the systolic blood pressure from 105 to 130 mmHg, and in the blood pressure amplitude from 25 to 55 mmHg by means of two O_2MT procedures of the variant KA 1 in a hypertensive man (aged 64) [106]. In the phase before the first alteration, drop in blood pressure repeatedly caused spontaneous circulation crises of the Ménière type. Pulse levels under these measurement conditions were between 66 and 72 before and after first and second alteration. (Procedure causes hardly any changes in pulse frequency, but pulse changes from weak to strong). This finding meanwhile reproduced in a large number of patients suffering from regulatorily conditioned hypertension should be monitored very carefully

Table 37 Measurements on dysregulated hypotensives before and after the 36 h O₂ multistep therapy procedure, variant GK 4-I (cure-like application; duration of each session 2–8 h; always combined with standard medication; repetition on consecutive days)

No.	Patient Name Sex	Age years	Σ t-O ₂ MT total number of hours	arterial resting P _{O₂} (mmHg) before therapy	after therapy	mean blood pressure (mmHg) before therapy	after therapy	Remarks
1	H.B. ♂	39	10 (with nicotinic acid)	—	—	105/75	125/75	
2	R.W. ♂	63	20	62	75	100/60	125/85	chain smoker
3	M.Ch. ♀	57	20	85	93	100/65	120/75	
4	R.J. ♀	52	20	85	95	105/70	120/85	
5	G.R. ♂	37	30	87	96	105/60	125/80	
6	K.Ch. ♂	34	30	81	89	105/70	125/80	
7	F.B. ♀	30	30	84	96	115/75	135/85	
8	B.G. ♂	48	30	70	90	110/65	125/80	
9	K.G. ♂	46	30	86	92	95/65	115/80	
10	G.W. ♂	58	30	75	92	95/70	110/80	
11	S.B. ♀	60	30	70	98	95/65	125/80	
12								
13	S.S. ♂	44	(1 year intensive exercise training)	(79)	(100)	105/75	125/75	for comparison

the feeling of great well-being which normally sets in a few hours after therapy, *greater exertions should be avoided in the first few days*, until the lasting increase in blood pressure amplitude has caused the formation of new cellular and energetic reserves.

When the blood pressure amplitude is permanently raised to over 200% in a relatively short time, as in Fig. 246, and the P_{O₂-art} is also rapidly increased, this is a *far-reaching change in the whole organism*. The patient's organs and tissues had, usually over many years, adapted themselves to the poor circulation by means of a more economic microtopography of vascularization and cell population in the intercapillary space, and then, suddenly, this excess — and that permanently! It would be a rewarding task to investigate the effects that such a rapid increase in blood pressure amplitude has on the various organs and tissues (increased mean

tissue P_{O₂}, reduction of pathogenetic factors). Individual observations of the alleviation of senile diabetes, reimplantation of loose teeth, the reduction of heart complaints etc. should make us thoughtful. It can be seen for the whole person that, after the lasting doubling of the blood pressure amplitude in older people who have suffered from hypotension for many years, their strain capacity, their energy and their mental performance capacity are greatly increased, i.e. *their vitality is significantly increased*.

Further investigation taught us that blood pressure and its amplitude could also be raised in patients with regulatorily conditioned hypotension with the GK 4-I therapy variant. Measurements of the results with this less intensive (milder), but therefore more time-consuming variant are compiled in Table 37.

5.2.5 Hypertension

We were stimulated to try to combat hypertension using O₂MT by a significant, basic physiological fact, i.e. that virtually the full level of the P_{O₂-art} is effective for the stimulation of O₂ metabolism in the vessel walls of the arteries and arterioles, and this arterial oxygen partial pressure is extremely strongly increased during the O₂MT procedures (cf. Fig. 7) and afterwards is usually significantly raised on a permanent basis. Hypertension is the sclerogenous

noxa with which, using experiments on laboratory animals, the non-specific mesenchyme reaction was found and the fast mesenchyme incorporation into the wall of the arteries examined [172, 194] (cf. Fig. 113). In the experiments on rats, acute arterial hypertension was artificially brought about by the subcutaneous injection of 1.2 mg hypertensin. It is known that hypertension in humans (diastolic blood pressure > 95 mmHg (12.7 kPa)

occurs spontaneously and at intervals, the frequency and duration of which rise in the course of time until the hypertension is fixed. An indication of the initial appearance of hypertension intervals was given above in the concept of the existence of a feedback (flip-flop) mechanism influencing the critical arterial vessel wall thickness. It is generally acknowledged that the fixation of the high blood pressure that can finally be observed arises due to degeneration of the arteries as a result of irreversible deposits (cf. Fig. 244). The life expectancy of a hypertensive person is dependent on the initial hypertensive intervals being diagnosed and effective therapeutic measures being undertaken (for hypertension and cerebral function disorders see [209, 385–389]). Numerous drugs to reduce blood pressure are today available for this, and this also seems to be one of the most interesting indications of the O_2MT . As discussed above, it can be assumed that the hardened, non-degradable deposits are formed in the arterial wall during the intervals of intensified mesenchyme metabolism there. In accordance with this concept *the combat of hypertension should take place by the use of the O_2MT to limit the intervals with high blood pressure as much as possible in terms of number and duration, in order to keep the time of the deposition phases short.*

In our experiment we began with a 36 h (18 day) O_2MT variant GK 4-I as soon as possible after recognition of non-fixed high blood pressure. In accordance with the given schedule, the duration of O_2 inhalation of the individual sessions of the treatment procedure is 120 min. In selecting the length of time it must be remembered that the breakdown of mesenchyme

in the artery wall is also a time-requiring process that possibly even takes longer than the mesenchyme incorporation, which is completed after approximately 60 min. We therefore recommend that the duration of the individual treatments should not be shorter than 120 min. It is necessary to determine the blood pressure immediately before, but also periodically during, treatment. These measurements repeatedly showed that *a considerable reduction in the systolic and diastolic pressure occurred as an immediate effect* even after the first sessions.

The treatment should take place during intervals without high blood pressure. Should it become apparent that the blood pressure increases considerably during treatment, then this suggests the involvement of spastic processes which can be intensified during treatment (see Paragraph 5.1.7). If such hypertensive episodes are observed, the treatment must be interrupted immediately and a more favorable time point waited for.

Results of treatments with the GK 4-I procedure are compiled in Table 38. In case No. 1 with pronounced but not yet fixed hypertension, the 64-year-old patient was quite determined to give up her job. The subjectively very strong improvement felt in her health after the O_2MT moved this patient to continue working for what is now 5 years. The values determined 5 years later without a further O_2MT cure are given in brackets in column 1.

Figure 247 shows a further impressive result of the reduction of the blood pressures in hypertensives after O_2MT , gained in independent in-

Table 38 Measurements on labile hypertensives before and after O_2 multistep therapy, variant GK 4-I (cure-like application; duration of each session 2 or 4 h; always combined with standard medication; repetition on consecutive days). When the O_2 status (particularly the PO_{2-art} at rest) could be elevated without interceptions, if possible, by means of the O_2MT variants GK 4-I or GK 2-I, an almost entire normalization of the RR values was achieved as a rule. Important findings!

No.	Patient		Age years	ΣO_2MT total number of hours	PO_{2-art} at rest (mmHg)		mean blood pressure (mmHg)		Remarks
	Name	Sex			before therapy	after therapy	before therapy	after therapy	
1	R.A.	♀	65 (70)	20 (no further therapy)	74 —	90 (83)	110/105 —	145/85 (145/70)	(5 yrs later)
2	M.H.	♂	50	20	79	100	175/115	165/110	
3	M.A.	♀	49	20	90	102	165/110	140/95	
4	K.E.	♀	70	20	83	95	160/95	145/85	
5	I.G.	♂	64	30	82	95	160/105	135/90	
6	v.A.B.	♀	61	30	80	102	175/110	140/80	already lasted more than 18 months
7	J.E.	♂	56	30	65	92	155/95	140/85	
8	J.E.	♀	59	30	69	85	155/95	130/80	

	age years	P_{O_2} -art O_2 MP		blood pressure RR before O_2 MT			blood pressure RR after O_2 MT			
		before	after	systol	diastol	amplitude	systol	diastol	amplitude	
No. of patients	N	26	27	27	27	27	27	27	26	
mean level	$\bar{X}$	70,08	69,08	89,00	187,96	92,41	95,56	154,26	78,15	mm Hg
standard deviation	S	$\pm 6,63$	$\pm 5,36$	$\pm 19,08$	$\pm 14,43$	$\pm 17,00$	$\pm 19,19$	$\pm 12,32$	$\pm 15,66$	mm Hg
t-test (significance)		-	a	b	c	d	b	c	d	

a,b,c,d: differences in the levels before and after O_2 MT statistically significant ($p=0,05$)!

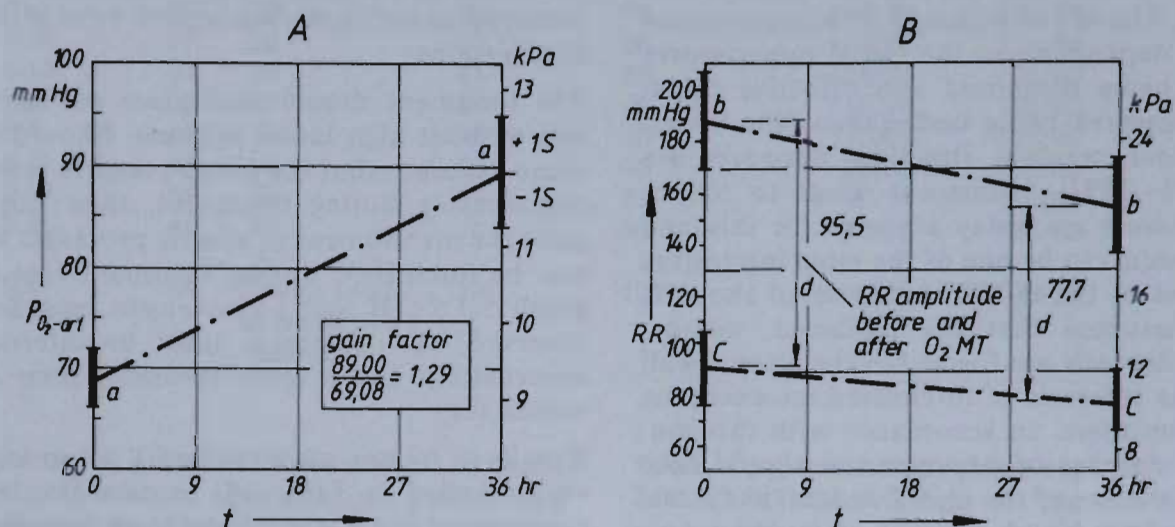


Fig. 247 Effect of the 36 hr O_2 MT procedure (variant GK 4) on the arterial resting P_{O_2} (A) and on the blood pressure (B) in 27 patients aged 70 ± 6.6 yrs with moderate to severe hypertension. Patients: Sanatorium Dr. Wolf, Bad Wildungen, FRG (N = 23). Augusta Klinik, Bad Kreuznach, FRG (N = 3). Hinzer, Bad Oeynhausen, FRG (N = 1)

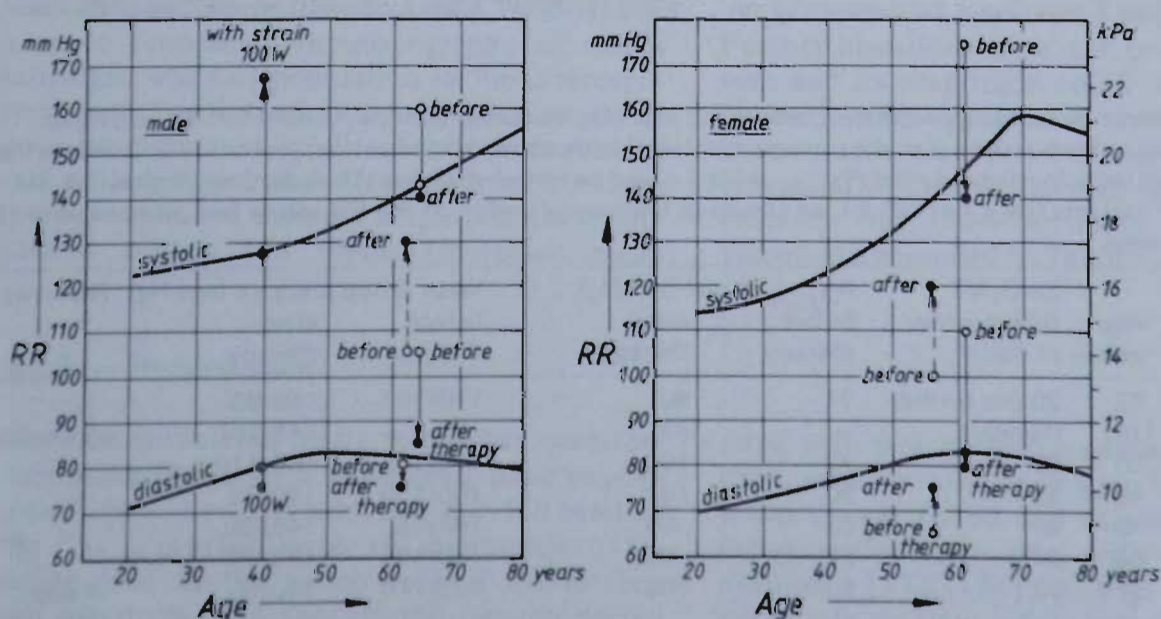


Fig. 248 Changes in the average systolic and diastolic blood pressure (RR method), at rest, with age, according to National Health Survey, cf. [32]. The measured values added show the renormalization of blood pressure in hypotensive (broken arrows) and hypertensive (solid arrows) patients through O_2 MT

stitutions. The above results are a challenge to the responsible medical practitioners to reproduce these findings and then to speak up for this new way to alleviate hypertension. The administration of drugs to reduce blood pressure was continued in almost all cases but their dosage could be considerably reduced in accordance with regular measurement of blood pressure at home (see also Paragraph 5.2.1).

In order to simplify the evaluation of the findings in hypertensives and hypotensives before

and after therapy, Fig. 248 shows curves of the *mean blood pressure as a function of age* (white population, USA 1962).

In connection with this it should be remembered that non-fixed hypertension can also be greatly alleviated by strict fasting (e.g. from 220/100 to 125/70 mmHg; mean values of 100 patients [350]). The indicated option of including a fast (cf. Table 42) as a 4th step of this variant can therefore lead us to expect an increased therapeutic effect.

5.2.6 Circulatory disorders

Circulatory disorders, which not infrequently lead to collapse, are dangerous, often fatal, effects of energy deficiency in weakened patients (old age, diseases, operation, radiation). Circulatory disorders are usually triggered when the O_2 offer to the body tissue (roughly corresponding to η), or the blood pressure amplitude in the daily rhythm pass through minima with critically low levels; also due to depressive influences. The permanent raising of the utilization coefficient of the O_2 binding capacity of the blood, η , (or of the blood pressure amplitude) by means of the O_2 MT procedure therefore results in an increase in circulatory reserves (cf. Fig. 46). The successful implementation of this therapy thus represents an *extremely effective preventive measure against circulatory disorders*.

In connection with this it was interesting to measure how a method used for centuries to stimulate the circulation — drinking coffee — influences the momentary level of the resting arterial and venous PO_2 . Figure 30 gave the answer with measurements on three healthy volunteers of different ages. After a depressive phase of approximately 20 min a strong increase in the PO_{2-art} is observed, lasting in our cases from roughly 30 to 240 min. The difference in the duration of the effect of 1:8 were in harmony with known experience of the individual variation in response to coffee-drinking. With the shorter duration of effect (case 57 years) an increase in the PO_{2-art} of approximately 15 mmHg (2 kPa) is measured. Furthermore a drop in the PO_{2-ven} of approximately 1 hour's duration was found. Coffee therefore temporarily increases the O_2 offer to all body tissue (including the myocardium).

It can be predicted that the findings in Figs 62 and 63 above will gain very great significance. They document the *discovery that the human organism can be led by variants of the O_2 MT in*

the course of 1 hour (15 min O_2 MT quick procedure GK 2-I) or of a few hours (O_2 MT short procedures GK 3, GK 3-I) from a condition of weakness (e.g. pre-collapses, conditions after fever or operations etc.) to a condition of strength with a multiplied provision of energy. This opens the door to a significant *acceleration of rehabilitation* after diseases.

The severest circulatory disorders often occur after tissue destruction (burns, radiation therapy etc.). In the radiation therapy of cancer, the flood of toxic degradation products from the destroyed cancer tissue and from the also destroyed normal tissue make it necessary to spread out the circulatory stress over many weeks by fractionated radiation divided over several treatment periods. The patients often die of circulatory failure, and not of their cancer¹. It must therefore be ensured with treatments of this kind that the decline in circulatory reserves is checked every few days by measurement of PO_{2-art} and PO_{2-ven} , at rest. A *favorable treatment planning for the individual case* can be derived from the course of the measured values. Most of all, however, *further indication for the O_2 MT procedure*, which causes an easily detectable restoration of the reduced η -value (i.e. the circulatory reserves), follows from these observations. Figure 249 shows a schematic presentation of this.

It is explained in [108, 391] that the risks of narcosis and operations in patients with circulatory lability and hence with low O_2 uptake can be considerably reduced if the O_2 MT procedure is started 2 weeks before the patient's operation.

¹ An advantage of the 1977 concept of the cancer multistep therapy emerges here, according to which the cancer tissue is isolated from the circulation by a selective obstruction of its blood vessels [22, 23, 120, 121, 125, 126]

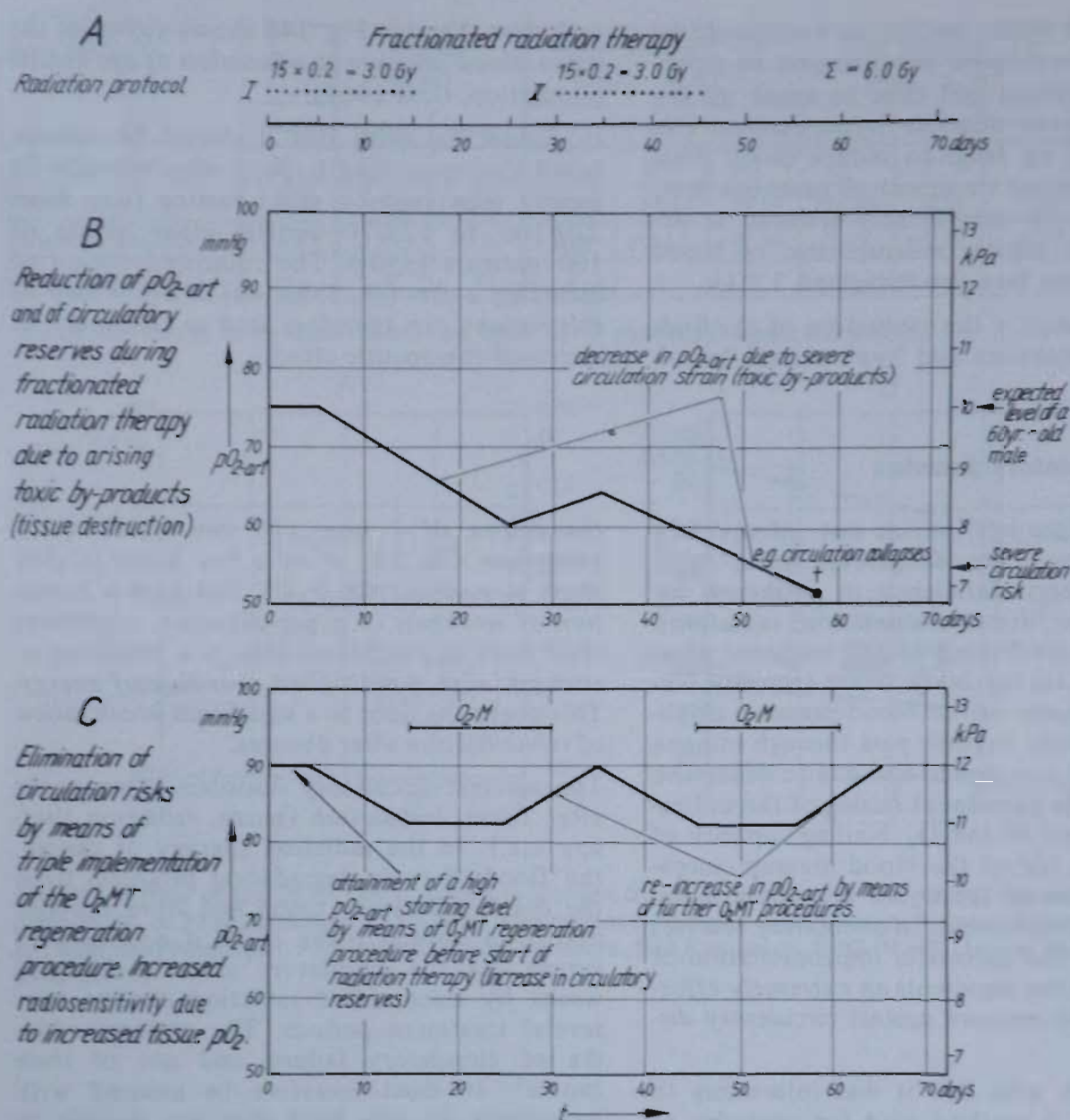


Fig. 249 Schematic presentation of the course of the arterial P_{O_2} during conventional fractionated radiation therapy of the lung carcinoma (A), in the type of treatment usual today (B) and in a new of treatment with triple implementation of the $O_2\text{MT}$ (C)

5.3 Combat of oxygen deficiency diseases

5.3.1 Conditioning by slow increase in exertion, increase in mobility and CO detoxification

It is frequently necessary or advisable to *prepare the patients* before or at the start of $O_2\text{MT}$, in order to increase their stress capacity and their mobility, and to optimize O_2 transport to the tissue via the bloodstream. The observation that the physical strain capacity rises quickly under O_2 application (cf. Figs 89, 125, 224) makes it possible to condition weakened patients for $O_2\text{MT}$ variants which would normally be contraindicated (variants

GK 1, GK 2-III, GK 4-II with Alupent) by the careful increase in exertion at the start of the procedure (under medical supervision). This conditioning with O_2 is of great significance in the $O_2\text{MT}$ obstetrics procedure, GK 2-IV.

A certain mobility is a prerequisite for the variants of the GK 2 group. It is often possible to produce sufficient mobility in physically disabled patients by means of the classical

Aid for persons impaired by chain smoking and car exhaust fumes

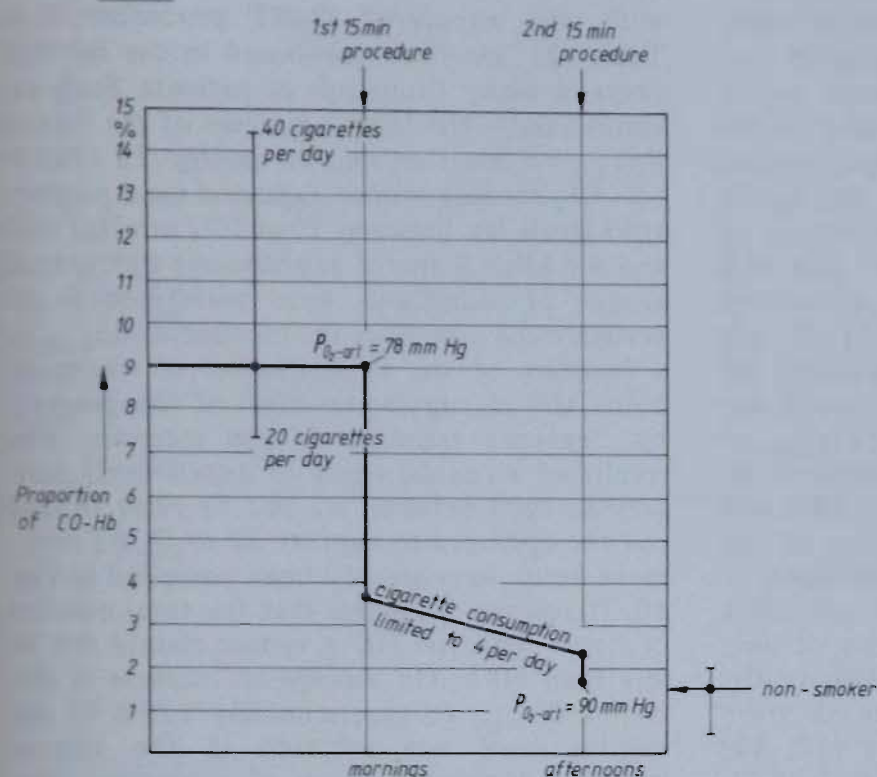


Fig. 250 Detoxication of hemoglobin in carbon monoxide poisoning by means of two 15 min O_2 MT quick procedure GK 2-I. Guiding levels

cures, mentioned in Paragraph 5.1.9. We should also think of *preprocedures with special drugs*. An example here is the successful treatment of chronic polyarthritis using s.c. applied interferon- γ , according to Obert and Hofschneider [392].

For patients damaged by chain-smoking or car exhaust fumes, conditioning by carbon monoxide detoxification is desirable. The CO poisoning of the hemoglobin leads to a reduction in the O_2 transportation capacity of the blood. The poisoning causes a reduction in the P_{O_2-art} , at rest, in the HbO_2 saturation, or the O_2 uptake of the organism, i.e. a deterioration in the O_2 status. In persons damaged by chain-smoking or car exhaust fumes, up to 15% of the hemoglobin can be excluded long term from the O_2 transport. The consequence is a critical deterioration in the O_2 supply of the organism. In chain-smokers consuming daily 20–40 cigarettes, we measured a fraction of 7.5–14.5% CO-Hb, using a Corning 2500 CO Oximeter (Corning Medical, Fernwald, FRG). The high poisoning quotas named, along with other overlapping harmful factors (cigarette paper, nicotine, bronchitis due to inhalation of smoke), explain some of the difficulties that limit the improvement of the P_{O_2} levels by O_2 MT specifically in chain smokers.

In the situation described it was important to find as simple a way as possible for detoxification. Detoxification in clinics has so far been undertaken in usually very costly hyperbaric chambers or with special pressure masks (e.g. hyperbaric oxygen mask from Ortho-Med Ltd, Edinburgh, GB) using O_2 with approximately one half atmosphere positive pressure, for at least 1 hour. Detoxification by means of two 15-min O_2 MT quick procedures GK 2-I, shown in Fig. 250, is simpler and less costly in terms of time and expense. It is only necessary to perform a fast detoxication in wards for hyperbaric oxygen for patients who cannot cope with exertion or who are disabled. As the figure shows, the fraction of CO-Hb drops from 9% after the first 15-min O_2 MT quick procedure and, after restriction of cigarette consumption to 4 per day, to 2.3%. After a repetition of the 15-min O_2 MT quick procedure with its high O_2 flow and its highly charged blood microcirculation, the CO-Hb falls to 1.5%, i.e. to levels that are, on average, found in nonsmokers. At the same it is sensible to convince such patients, by demonstrating data like those in our figure, of how greatly their O_2 status, i.e. their energetic status, can be raised by restricting their cigarette consumption.

5.3.2 Lungs and the partial regenerability of their arterialization system

The lungs and particularly their *alveolar-capillary O₂ diffusion system* (arterialization system), shown in Fig. 26, would seem to be primary targets of the O₂MT, according to the previous paragraph. The senile-emphysematic alteration of the lung, typical for the ageing human, is characterized by the restriction of the alveolocapillary gas exchange area and distribution disorders, leading to a reduced pulmonary O₂ diffusion [393, 394]. It has already been shown above how severely the maximum O₂ diffusion capacity sinks with age (cf. Fig. 123 A) and how greatly the PO_{2-art} , at rest, drops with age due to deterioration of the cardiopulmonary performance (cf. Figs 28 A and 32). Theoretically the observed drop in the PO_{2-art} can be conditioned by deterioration of several lung function parameters (deterioration of alveolar ventilation V_A , reduction of lung circulation BF, drop in diffusion capacity D_L and, more than anything, *increase in their regional ventilatory inhomogeneities* [32, 80] and in the shunt volume (see Paragraph 1.1.8.7). The main contribution probably stems from the increased shunt volume and from the increasingly uneven distribution with age. The non-specific mesenchyme reaction (cf. Fig. 26) could also be of direct influence here. From pathology we know that in lung edema, chronic blood congestion etc. the diffusion length is enlarged from normally approximately 1 μ m to 5–10 μ m. For changes in the lung caused by disorders of the pulmonary gas exchange due to restrictive lung diseases, and examination of them using the *distribution analyses* of ventilation, perfusion and O₂ diffusion capacity, see [395, 396]. The clarification, i.e. with the method described in [80], of the changes in the arterialization system of the lung that occur with age or after O₂MT, is a very topical task that is being worked on. It is certain that, due to the close coupling of the cardiac and lung systems, a deterioration in cardiac performance is both cause and consequence of a reduced lung function. The measurements and findings compiled in this book show a surprisingly high reactivity of the lung-heart system (abbreviated as LH system). As described more closely in Fig. 29, the reactivity of the LH system can be characterized with at least two time constants (τ_1 = a few seconds, τ_2 = some hours).

Our unexpected discovery that the *discussed drop in PO_{2-art} , at rest, with increasing age is of a largely reversible character* [3] and that a *regeneration of the degenerated LH system with very long-lasting effect can be achieved*

with the discovered O₂MT procedure (e.g. Table 27), has been confirmed in the last few years in many thousands of patients. Such examples show the *lasting increase of the resting PO_{2-art} to levels around 90 mmHg (12 kPa) in 60–70-year-olds* whose expected (and pretherapy) levels lay between 75 and 72 mmHg (10.0 and 9.6 kPa). Series of experiments with several groups of individuals were performed to investigate the course of the increase in PO_{2-art} as a function of the total number of treatment hours and in supplementation of the program by "exercise training" in the intervals. The results of a *special series of experiments with persons aged between 37 and 73 years to find out the appropriate number Σt of O₂MT treatment hours* have already been compiled in Fig. 40. It follows from this that the total number of hours with the GK 4 variant should not be less than 30 h. On average an increase in the resting PO_{2-art} to approximately 117% of the starting level was achieved in the heterogeneously composed group of volunteers after 30 treatment hours. *When restricted to persons over 60 years the increase was roughly 130%.* The increase continues somewhat even after 30 h, whereas after an *average treatment time of 36 h*, which was recognized as appropriate, the *mean level* mostly observed at the end of therapy is reached, i.e. an PO_{2-art} of almost 100 mmHg (13.3 kPa) at rest. Only very rarely did the attainable final level in these tests lie below 90 mmHg. *The therapy failed in $\leq 15\%$ of cases.* We were often dealing here with patients whose respiratory regulation was clearly controlled by O₂ deficiency (Loeschke), see also Paragraph 1.1.8.6.

Figure 251 shows a compilation of individual examples of the course of the PO_{2-art} , at rest, as a function of the number of therapy hours. The curves suggest that the meaningful number of hours is greater with low starting levels than with high (only light variation in the gradient $\frac{dPO_{2-art}}{d\Sigma t}$ of the increase).

The picture given by the results entered in the summarizing presentation (Fig. 251) is still too unsatisfactory. This statement follows from *control measurements of the PO_{2-art} undertaken during the treatment*. These measurements revealed that these values were not as they should be, i.e. between 125 and 160 mmHg (almost double the level when normal air is breathed), but in most cases considerably lower. The cause of this was partly a too low

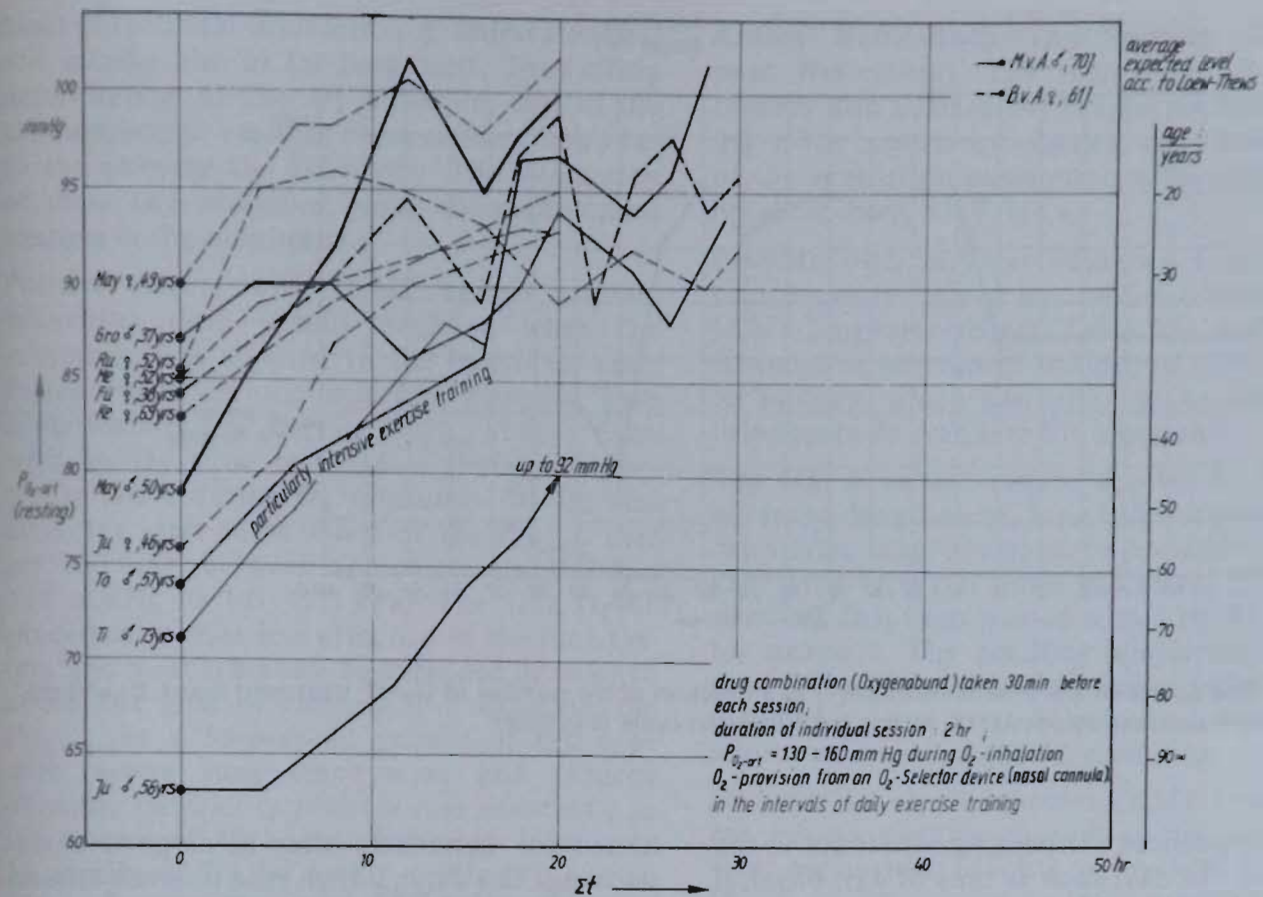


Fig. 251 The course of the arterial resting P_{O_2} as a function of the total number of O_2 MT treatment hours Σt in individuals with very different starting levels (examples). Measurement time ≈ 10 a.m.

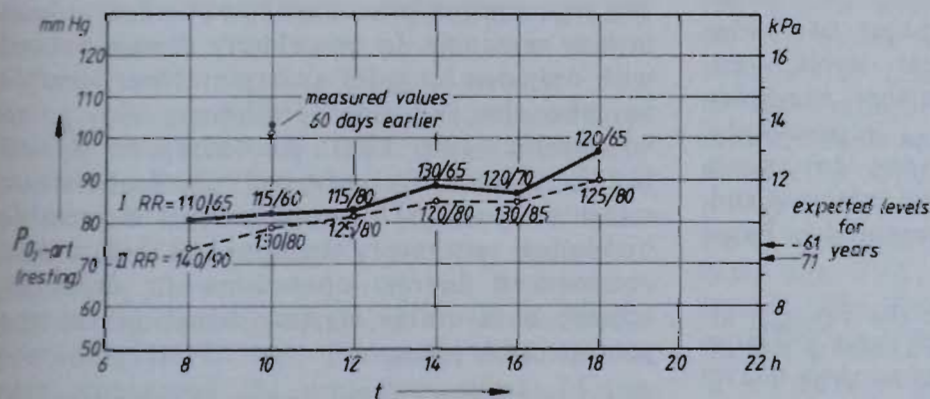


Fig. 252 Daily profile of the arterial P_{O_2} (the corresponding blood pressure values are added during a working day in a 71-year-old male (I) and a 61-year-old female (II), whose O_2 MT effects had greatly diminished approximately 19 months after their last treatment. (In I the stimulus which triggered the drop was slight smoke poisoning)

flow rate of oxygen added, and insufficient observance of the instruction (at that time) only to inhale via the nostrils during the procedure. From this can be seen the superiority of mask applicators and also how important it is to undertake controls during the procedure. The results in the diagram roughly correspond to the circumstances that exist in practice at the start of training in the application of the O_2 MT. When the procedure is ideally performed the steepness of the rise in the P_{O_2} -art, at rest, with the number of treatment hours should be somewhat greater and hence the

total number of treatment hours required somewhat smaller than that given above. In connection with this a *blind experiment* of an at first unintended kind should be mentioned. In one group of volunteers (experiment as in Fig. 251) there was no apparent rise in the P_{O_2} -art, at rest, over a timespan of approximately 16 h of therapy. Checks showed that there was a defect in the device, and the volunteers had inhaled normal air.

The daily fluctuations which overlap with the increases are an expression of the reactivity of this characteristic value of the health status,



Fig. 253 The course of the arterial resting $PO_{2-*art*}$ as a function of the number of O_2 MT treatment hours Σt and the response to a vaccination against flu during the treatment cycle (example)

and consequences of changing conditions in the course of the day, such as time of day, physical activity, stress etc.

Figure 252 shows the daily profiles of individuals in whom the effect of the 36 h O_2 MT procedure GK 4-I on the $PO_{2-*art*}$ was already considerably reduced due to noxae. It is striking that, in this transitional phase of fading therapeutic effect, the highest levels were measured in the evenings. Further examples showing the alterations in $PO_{2-*art*}$ in previously successfully treated patients, due to excess stress with lack of exercise, a cold infection and 14 day exercise training are presented in Paragraph 1.1.8.2.

It is interesting that a drop in the $PO_{2-*art*}$, at rest, of, e.g. 10 mmHg (1.3 kPa) and a rise in the $PO_{2-*ven*}$, at rest, of 7 mmHg (1 kPa), i.e. a considerable temporary deterioration of the O_2 status, was measured in the male partner for a duration of approximately 96 h after sexual activity. A further finding on the high reactivity of the resting $PO_{2-*art*}$ is the steep fall in this characteristic after vaccination against influenza during therapy shown in Fig. 253.

In a 63-year-old patient who had been a *chain-smoker* for over three decades we found particularly low levels of the resting $PO_{2-*art*}$, which is so characteristic of the lung function, (around 60 mmHg $\hat{=}$ 8 kPa) and, initially, only a moderate increase (to levels around 70 mmHg $\hat{=}$ 9.3 kPa) after the application of the GK 4-I therapy variant. In this case the severe deterioration of cardiopulmonary performance con-

tinued for some time after he stopped chain-smoking. The $PO_{2-*art*}$ then rose to levels around 80 mmHg (10.6 kPa) and could not at first be further increased by O_2 MT. A strongly reduced $PO_{2-*ven*}$ was usually measured in patients with particularly low $PO_{2-*art*}$ (counter-regulation).

The regeneration procedure can be of great help in *lung resection*. In one elderly female patient with only one lung, for example, it was possible to raise the very low pretherapy $PO_{2-*art*}$ to 95 mmHg (12.6 kPa). According to Krauss [397], individually adapted physical-dietetic measures (or O_2 MT, supplemented if possible by clinical respiratory therapy) [102] should be commenced before operations, in order to achieve a favorable starting situation for the postoperative phase.

The direct effects of the extremely high alveolar and arterial PO_2 should also play a part in the combat of lung diseases using O_2 MT. The medical literature [352, 353, 398] already contains numerous, mostly positive experiences and reports of successful attempts to combat the consequences of *lung emphysema* and *chronic bronchitis*, especially in older patients, with oxygen. A typical feature of both diseases is the emergence of *cor pulmonale* (high blood pressure in the lesser circulation) which leads to reversible arteriosclerotic changes in the walls of the vascular system of the lung. The main cause of the high blood pressure in the pulmonary circulation must be regarded as an O_2 -deficient supply to the arterial blood vessels, mainly caused by reduced performance of the

heart (functional disorders, e.g. mitral stenosis) and usually also of the lung itself. The further deterioration of the O_2 situation due to the arteriosclerotic vascular degeneration then adds to the primary O_2 deficiency. The interaction of these two processes causes the pathological changes in the lung space.

Positive effects with O_2 MT against *chronic bronchitis* were usually achieved when the procedure was adapted to the individual case. Patients with chronic bronchitis normally have a particularly low starting PO_{2-art} at rest. Even with an O_2 flow set at 4–6 l/min, *measurements taken during O_2 inhalation* 20–30 min after the start show levels of the PO_{2-art} that are too low, between approximately 105 and 115 mmHg (± 14 –15.3 kPa). The 36 h O_2 MT procedure is then less effective in the lung system and must therefore be extended in order to attain the goal of therapy. For example, the PO_{2-art} in a 54-year-old patient of this type with severe lung emphysema and reduced dynamic respiratory reserves rose constantly in the course of 40 hours of therapy from only 58 mmHg (7.7 kPa) to 80 mmHg (10.7 kPa). The procedure was then further continued up to a total of 60 h, and a further increase to near the therapeutic target level took place. In individual cases the procedure should therefore be extended and continued until the procedural target level of 90 mmHg (12 kPa) has virtually been reached. The total numbers of hours required will therefore vary somewhat from case to case, and can be roughly estimated after 20 h of treatment from the resulting increase in the resting PO_2 . The procedure can generally be performed more effectively if the first treatments are accomplished with a somewhat higher O_2 flow (4–6 l/min) and if it is supported by special measures or immediately preceding HOT* (see Paragraph 3.3). In the case mentioned the subjective effects of the treatment were particularly impressive: a sensation of dizziness which had been constantly present for 10 years, virtually disappeared, as did also a dull pressure in the head. A tingling sensation in hands and feet was completely eliminated. There was a striking increase in physical performance capacity. In the application of the procedure against chronic bronchitis, standard treatment (expectoration, moistening of inhalation air etc.) should not be omitted (Wolf, Bad Wildungen, FRG).

It is particularly advisable for patients with the beginnings of chronic lung insufficiency to supplement the obligatory exercise training of the O_2 MT procedure by daily *thorax and respiratory-physiological exercises* (experiences of

Krauss Berlin-Buch, and Neubert, Hoheleye near Winterberg). The increase in PO_{2-art} is thereby also utilized for the lasting strengthening of the inspiratory muscles, and a restoration of the ventilation parameters of the lung occurs (vital capacity, RMV, etc.).

Patients with very far advanced lung insufficiency can be helped by the GK 6 variant, the O_2 MT long-term aid (cf. Table 31), and by the frequent or permanent utilization of the O_2 MT technology, which can often make life worth living again or even save life altogether.

The GK 6 variant can be applied in cases of advanced lung cancer, lung tuberculosis and in cases after lung resection. In bronchial asthma [399] the O_2 MT is more successful if the patient has first been treated with 3 HOT* cycles, for example. The resulting alleviation of dyspnea offers the patient with severe pulmonary insufficiency very great help, with a significant improvement in his general condition.

In order to check whether O_2 MT treatments can achieve positive changes in the lung function parameters (doubts expressed by Petro [400]) we have so far, on the suggestion of Caspers, performed "small spirometry" using the Spirotron 2 device (Drägerwerk, Lübeck, FRG) on 15 patients. The results were mean improvements in the *peak flow* (PF) of +15.5 % and in the *forced vital capacity* (FVC) of 240 ml (± 6.5 %) due to O_2 MT. The *forced expiratory volume* (for 1 second) (FEV_1) hardly changed in our groups. Caspers [400a] undertook measurements with the same device on 171 patients after O_2 MT (some also with respiratory therapy). An improvement in the FVC and FEV_1 occurred in 61 % of cases. In 27 % of cases the FVC, but not the FEV_1 , was improved. *The discovered increases in the maximum PF and FVC respiratory function parameters and, partially, also in FEV_1 , represent a significant reserve for the increased demand on the ventilatory function and increase the amplitude between maximum ventilation and ventilation at rest.*

Additional preparatory therapeutic measures are necessary also to improve the FEV_1 in patients with bronchial asthma, chronic bronchitis and other obstructive lung diseases. An aerosol inhalation of medicaments causing detumescence of the mucous membrane and dilation of the bronchus, e.g. using the IPPB S 2 respirator (Meyer, Bad Ems, FRG) and intermittent hyperbaric treatment are useful.

Stimulated by Krauss and by the results of respiratory-physiological studies into respiratory feedback in the Erwin Braun Institute (Engel-

berg, Switzerland) in 1979, we have since included "respiratory therapy" as an *adjuvant step* to economize the respiratory process in special cases (effect: increase of PO_{2-art}).

The functional regeneration procedure for the lung-heart system also seems to raise the *vocal performance capacity* significantly, when caught in decline, as the following example shows: an internationally famous singer, always on the go, came to us at the age of 53 years, complaining that his vocal performance capacity was beginning to decline. Measurements showed that his PO_{2-art} , at rest, had already dropped to 72 mmHg (9.6 kPa), certainly due to the permanent excessive stress of his tours.

5.3.3 Central nervous system

In order to assess the therapeutic potential of the various O_2MT variants it is necessary to know the *peculiarities of brain metabolism and its regulation*. By comparison with the mean specific energy turnover of the tissue of the human organism, the specific energy turnover of the brain tissue is known to be larger by a factor of approximately 10. A suitable characteristic value for the level of the energetic status in the brain is the concentration of the energy-rich phosphates adenosine triphosphate (ATP) and creatine phosphate (CP) in the brain cells. It is known that an increasing deterioration in the brain's energetic status leads to phenomena such as increasing fatigue, increasingly weakened memory [402], reduction in mental performance capacity, certain symptomatic psychoses and delirious states [192, 209, 387]. The progredience in the above chain of phenomena shows that the mechanism of specific access to the information store elements of the brain fails more and more with increasing cerebral energy deficiency. This switching mechanism evidently requires more energy. Figure 254 shows a diagram of the reduction of memory with age in normal persons [389].

The energetic status of the brain, i.e. the synthesis of the energy-rich phosphates, depends mainly on the metabolism of glucose and oxygen in the brain tissue. The extent of the glucose metabolism in the brain is known to be limited and kept roughly constant by the blood-brain barrier (BBB, see Paragraph 1.4.10) [192]. Without this regulation, the rise in blood glucose concentration could lead to a critical increase in the proportion of naturally occurring aerobic glycolysis of the nerve cells (8%) [403], and the normal pH of the brain tissue

This value was then raised lastingly to 95 mmHg (12.6 kPa). Some weeks later our singer claimed that he had never before achieved such good performance when recording, and a music critic wrote of him: "X, who seems to be experiencing a new vocal blossoming, surpassed himself vocally and dramatically. We seldom hear the words so resonant, metallic and yet measured in expression." Ergometric and CO_2 production measurement of the lasting increase in physical performance capacity due to O_2MT procedures have already been reported above. According to analogous observations in other singers of this age group, the lasting increase in physical energy also seems to make itself strongly felt in vocal performance capacity.

(≈ 7.0) could further drop to levels that trigger irreversible brain damage [2, 403]. Due to the limiting effect of the BBB, glucose as the major substrate of the brain metabolism forms the bottleneck. The most important thing in disturbance of the brain's energy balance is therefore usually to strengthen or renormalize the penetration of glucose over the BBB.

Pharmacological methods which can contribute to the performance of this task can be found in the cure-like application of substances such as pyridinol (Encephabol) [400], Curantyl and nicotinic acid [192]. There are reports [404, 405] on the raising of the pathologically reduced brain glucose metabolism from 22.5 to

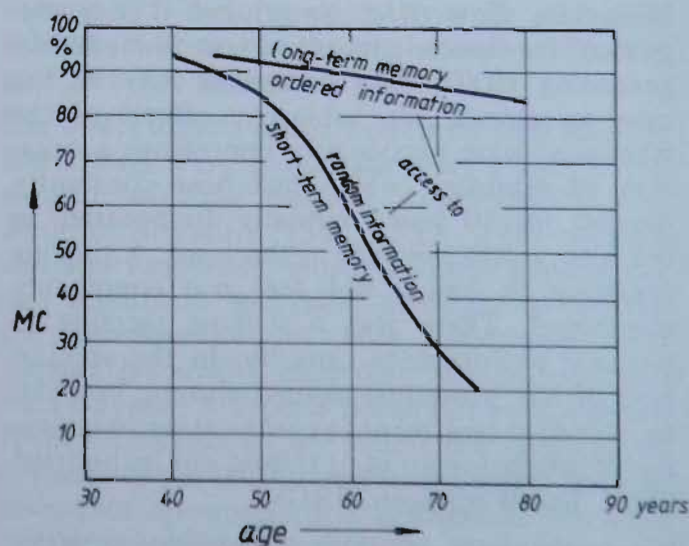


Fig. 254 Quantitative presentation of the decrease in memory capacity with age. The effectors involved. For improvement of the access ability through O_2MT see [406]

82.2% of the normal level in a 25-year-old woman with amnesia, and from 29 to 120% of the normal in a 51-year-old man diagnosed with "cerebral arteriosclerosis", simply by the administration of pyridinol (daily dose up to 1.2 g) over 36 and 33 days, respectively.

According to Schmidt (Institute of Pharmacology and Toxicology, Medical Academy, Dresden, GDR) mental capacities which once existed can normally be regenerated with the following combination of drugs: 1. pyridinol (Encephabol) with the dosage given above; 2. piracetam; 3. neclophenoxate; 4. methyl glucamine orotate or magnesium orotate. We could also emphatically refer the reader to the administration of calcium antagonists (Nifedipin, Sibeliun) for the therapy of cerebral function disorders (in combination with O_2MT).

Fischer [405a] reports on a process for the *self-assessment of slight forms of cerebral insufficiency*.

Hardly any notice has so far been taken of the further method of greatly improving the energy balance of the brain by stimulation of the oxidative metabolism over greater or lesser periods of time, or even lastingly [2, 106, 212, 213, 260]. The concrete means for this is either the single application of the O_2MT , by which, according to Table 13, the concentration of energy-rich phosphates in the brain can be significantly increased, or the cure-like 36 h (18 day) O_2MT procedure GK 4-I.

In the selection of therapy patients, the following basic physiological facts must be considered: whilst the glucose penetration through the BBB is held virtually constant, when the blood glucose concentration changes over the broad range of 80–800 mg/100 ml, the oxygen transport to the brain, according to most recent measurements by Hollmann (cf. Table 15) rises

considerably (by about 30%) when the cardiac output is increased fivefold by strenuous physical activity. A certain counter-regulation of the cerebral circulation occurs due to constriction of the resistance vessels with increasing blood pressure. In order for the therapy effects to be released in the brain it is essential that the *mentioned increase in circulation and hence an increase in the PO_{2-art} [229] and in the brain metabolism do occur in physical exertion and in or after O_2MT* . Further details of the O_2 supply to the brain are dealt with in [386].

Variants of the O_2MT to be given preference for the improvement of the metabolic and energetic situation in the brain are the KA 1 variant: 80 min O_2MT nicotinic acid procedure (cf. Table 32), the 36 h O_2MT variant GK 4 (cf. Table 27) for therapeutic purposes, and for prophylaxis the 15 min O_2MT quick procedure (cf. Table 25).

On the subject of the high dose of nicotinic acid in the KA 1 variant, according to various literature references, the nicotinic acid does not directly increase the circulation in the brain itself, but rather the stimulated circulation in the whole of the upper half of the body has a positive influence on the brain metabolism [387]. We have found that a very great increase in the effect of the O_2MT occurs in the head and neck region due to the nicotinic acid. In connection with this we should also refer to the dilation of cerebral vessels by inhalation of amylnitrite (cf. Table 16, column 1.1.4).

On the basis of [180, 182] the perlingual administration of g-strophanthin (biteable capsule, 6 mg, 6% solution) is intended as a further drug to improve brain metabolism in the KA 1 variant, not so much because of its cardiac effects as because of its effects in the brain area, which are the object of growing interest among neurologists.

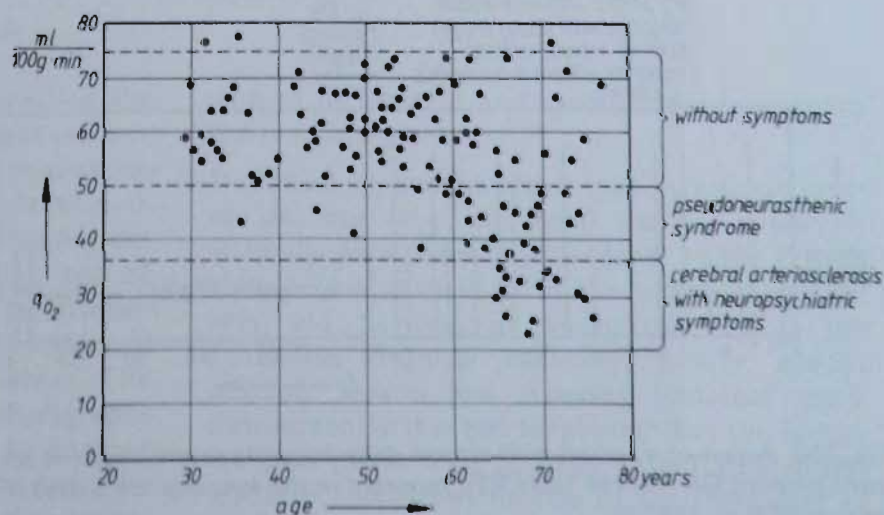


Fig. 255 O_2 consumption of the brain ($\sim$ cerebral blood supply) dependent on age. Appearance of severe cerebral arteriosclerosis from approximately 60–65 years [387]

Chronic or suddenly occurring O_2 deficiency can be regarded as the primary cause of most brain diseases. Thus the frequency and severity of cerebral arteriosclerosis increase rapidly after the age of 60, with the given drop in cardio-pulmonary performance, as Fig. 255 shows. Paragraphs 3.4.4, 5.2.2 and 5.3.9 comment on the combat of cerebral arteriosclerosis by elevating the PO_{2-art} , at rest.

When there is chronic O_2 deficiency in the brain, particularly with cerebral arteriosclerosis, we urgently advise that the 36 h O_2MT procedure, GK 4-I variant, be supplemented by a cure beginning on the first day of treatment and continued over 60 days, with a dose of pyrrithinol (*Encephabol forte*) three times daily, and also a dose of the other three drugs of the Schmidt's combination named above.

Despite the described regulatory mechanism, which attempts to keep the substrate offer to the brain tissue constant, the results of experiments compiled in Fig. 133 prove that the direct effect of O_2MT is surprisingly strong. This observation of the great increase in the energy-rich phosphates in the brain during O_2MT is of principal significance for the assessment of the general potential of this therapy. This result also answers the question of how long it takes after the end of therapy for the concentration of energy-rich phosphates, stored during the O_2MT treatment, to drop again roughly to its initial level. It follows from the given diagram that the concentration of these phosphates is still approximately 10% higher than the initial (normal) level 4 hours after the end of treatment. This result has led the author to recommend experiments with a 90 min O_2MT procedure immediately before foreseeable severe strain (e.g. before major brain operations).

It can also be assumed that there are direct effects on the function of the regulatory centers in the brain during the O_2MT procedures.

When the body temperature rises very sharply (high fever, whole body hyperthermia with high temperatures), according to [388], a discrepancy between the glucose requirements, which rise quickly with the temperature, and the glucose offer via the BBB, which rises more slowly, occurs in the brain for about 20 min. Psychic irritations (tendency towards psychoses, febrile delirium, increased irritability in the sensory field) are observed during this glucose deficit. An observation from experiment, important for our theme, is that these *psychic irritations do not occur with O_2MT measures*.

It is also worth mentioning individual observations, as presented in Fig. 256, of the *striking reduction in the frequency and severity of certain types of migraine after O_2MT cures*. The application of the O_2MT is contraindicated during migraine attacks, as the therapy has been repeatedly seen to *intensify the spasms* acutely.

The observations of a statistically significant improvement in the Wechsler's memory quotient by means of treatment similar to the O_2MT procedure, described in [406, 407], and the observations of a *great reduction in reaction times* after O_2MT , discussed in Paragraph 1.1.5.9, deserve particular consideration.

"Brain jogging" (training of attention, alertness and concentration, training of the basic memory functions), as described and studied by Fischer [408], can be recommended as an adjuvant O_2MT step to increase mental performance activity. In connection with this we would refer the reader particularly to Lehr and Fischer's *psychopathometric tests for cerebral insuffi-*

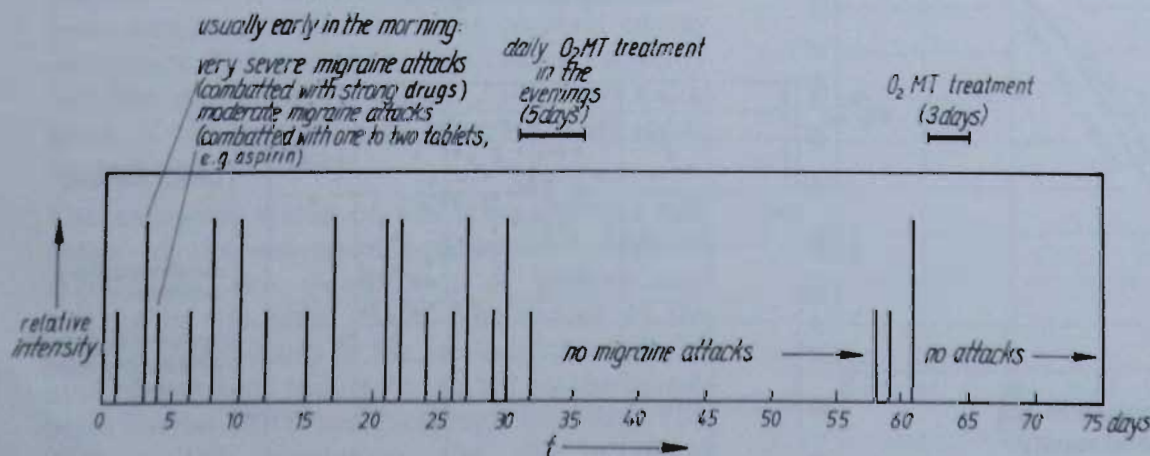


Fig. 256 Arrest of a period with almost daily occurring severe migraine attacks by means of a 36 h O_2MT treatment (variant GK 4-I, see Table 27), repeated in the evenings for 5 days. Female patients, 59 yrs, slight hypertension (RR $\approx$ 155/95)

ciency [409–411], which seem to be excellently suited to prove the cerebral effects of O_2 MT (information-psychological basic values: short storage capacity and influx of information to the preconscious memory improved).

There are also numerous observations of the reduction in *sleep disorders* after lasting restoration of the O_2 uptake. According to [412], further aids are L-tryptophan tablets, or a large glass of warm milk at bedtime.

An important indication of the O_2 MT is the *reduction of the probability of strokes*, e.g. by the timely alleviation of hypertension and degeneration of the vessel walls. Kern's as yet unpublished methods to prevent strokes and reduce their consequences should be mentioned here.

Paragraph 4.2.5 has also referred to the chance of, under favorable conditions, being able to alleviate the disrupted functions of severe spontaneous circulatory disorders (functional stenoses, embolism, hemorrhage) by the immediate application of certain variants of the O_2 MT. Not least should the utilization of the O_2 MT sleep or of O_2 MT cures be thought of in the rehabilitation phase after severe spontaneous circulatory disorders in the brain. The gradual elimination of late effects of impaired blood supply in the brain seems, in accordance with various observations which have been reported to the author, to be a particularly interesting field of the O_2 MT.

In anesthesiology it is advisable to perform the O_2 MT in the weeks before narcosis with greater than average risk, and thus contribute to the stabilization of the blood-brain barrier and the circulation by the powerful increase in the O_2 status [108, 319].

Whether the O_2 multistep therapy also can or

does help against psychic lability (e.g. schizophrenia, depression) has not yet been investigated; however, the observation of the arrest of psychic irritations with steep increase in body temperature, and the inverse indication that influenza infections frequently trigger psychic episodes due to the sharp drop in η , combined with first communications of a considerable alleviation of confused stages after the O_2 MT, entitle us to be hopeful. We can at least expect a prophylactic effect against organ damage if psychopharmaceuticals with (not fully avoidable) side-effects are taken over many years.

Observations of a *considerable reduction in tremors* in a series of *Parkinson patients* after O_2 MT should be followed up further (Zerlauth, Klagenfurt, Austria). The same applies to individual observations of an *alleviation of complaints in polyneuropathy syndrome*.

Multiple sclerosis (MS, encephalomyelitis disseminata), which attacks the myelin sheath (cf. Fig. 120), is a great, as yet unsolved problem of medicine today. Multiple observations of the triggering of MS attacks after phases of severe O_2 deficiency (e.g. influenza (cf. Fig. 63), severe drop in η) and English observations of the *disappearance of severe MS symptoms after treatment with hyperbaric oxygen* force us to conclude that O_2 deficiency plays a negative role in the as yet unknown mechanism of MS. This recognition challenges us to investigate the effect of intensive variants of the O_2 MT (e.g. variants GK 4-II and GK 7) on multiple sclerosis.

The findings and observations discussed here and in Paragraphs 1.4.10, 4.3.1 and 5.2 should stimulate thorough investigations of the therapeutic potential of the O_2 MT concept in the cerebral region.

5.3.4 Sense organs

O_2 deficiency of the eye. O_2 deficiency is the primary cause of a series of eye diseases (retinopathies, cataract, indirect also glaucoma, excessive light sensitivity, sudden deterioration in visual acuity). In most cases this deficiency occurs as a result of the drop in PO_{2-art} and of circulatory disorders, conditioned by arteriosclerosis of the supplying vessels and advanced inhibition of the blood microcirculation. The aspects and methods discussed in Paragraphs 5.2 and 5.3.3 can largely be used to combat this type of ocular circulatory disorders. We can therefore restrict ourselves to the discus-

sion of differences and specific standpoints for the ocular region.

It should be remembered that in various areas of the eye (e.g. the lens) the O_2 supply is virtually determined by the level of the PO_{2-art} alone. This accords with the observation that very old persons, in whom the PO_{2-art} has generally dropped critically, nearly always develop severe eye diseases (cataract etc.). Consequently it is not surprising that the lasting increase in the PO_{2-art} after O_2 MT procedures leads to significant success in the treatment of

not yet irreversible eye damage. Thus, for example, patients often reported the disappearance of the initial stages of cataract after O₂MT. In extensive discussions on the causes of cataract [184], the drop in the PO_{2-art} in old age is not usually mentioned.

Ophthalmology has the advantage that optical observations of the eye-ground can immediately recognize changes in the vessel system, for example. It is therefore of pioneering significance that ophthalmology, after earlier doubts (see here also Paragraph 5.3.3, nicotinic acid), now admits and even utilizes the *possibility of vasodilation by means of specific drugs, even for the brain and the ocular system attached to it* [185].

As long as no irreversible damage to the optic nerve fibers and retina cells has occurred, a relatively slight increase in the O₂ status (restoration of a reduced PO_{2-art} at rest, Fig. 251) and in the η -value are often sufficient to transform the diminished metabolism back to full function. The 80 min O₂MT nicotinic acid procedure, KA 1 variant (cf. Table 32) should be seen as particularly suited for this. Great therapeutic, long-lasting effects have also been found after the application of the 36 h O₂MT variant GK 4-I and the 15 min O₂MT quick procedure, GK 2-I variant (cf. Tables 27 and 25). There are already many impressive individual observations of an improvement in retinal circulatory disorders in older patients (e.g. 73-year-old male, PO_{2-art} at rest, raised from 72 to approximately 90 mmHg) and also of the elimination of visual field defects and of sudden changes in visual acuity. The administration of Pentoxifyllin (Trental, Trental 400) both i.v. and orally [413] has proved its worth as an adjuvant step to improve blood supply of the retina. The case of a female patient who was extremely light sensitive, always had to wear dark glasses and could no longer watch television, was particularly impressive. The high degree of light sensitivity disappeared immediately after completion of the O₂MT procedure. She no longer needed her dark glasses and could once more watch television regularly. In another case (Krutoff, Munich, FRG), an 84-year-old patient reported that for some time he had only been able to read if he used glasses and a magnifying glass at the same time. After the O₂MT cure he could read using a pair of glasses that he had laid aside 10 years before. The optical data that had existed for him 10 years previously had returned. There are several other examples along these lines where new glasses became necessary after O₂MT and, to the amazement of the optician, lenses with less refraction were

again sufficient. There were reports by Meixner (Villingen, FRG) of some cases of elimination of glaucoma by means of normobaric O₂MT. Observations on the reduction in intraocular pressure due to the treatment in the hyperbaric chamber or with O₂ application at a flow rate of 15 l/min [414] make the application of the O₂MT excess pressure quick procedure, GK 7 variant, seem to be strongly indicated against glaucoma. These experimental observations carry great weight because they prove the reversible character of this type of eye disease caused by oxygen deficiency.

g-Strophanthin is often included in the drug combination to alleviate ocular O₂ deficiency. That this cardiac glycoside, in addition to its main effect on the myocardium, also has a peripheral effect and, more than anything, positively influences the cerebral metabolism, is emphasized in [185] and [418]. It was proved in [186] with radioisotope angiography in animal experiments that the glucose concentration increases in all examined parts of the brain under the influence of g-strophanthin. More importantly, it has recently been proven using the Xenon clearance method that in both deficiently and sufficiently supplied brain tissue, the circulation is significantly improved even when there is no manifest cardiac decompensation. From the viewpoint of these experimental findings, the results discussed in Paragraph 2.2.1 [148, 420] of the reliable effect of perlingually administered g-strophanthin, are of great relevance and interest.

The practice and utilization of the O₂MT in ophthalmology have begun. Measurements of the (lasting) influencing of critical flicker fusion have been initiated. After the good results obtained in our Institute and by many O₂MT partners, this field of application is indisputably a rewarding one. It is therefore advisable to establish contacts with ophthalmologists in order to arrange the continuous admission of respective patients to specialized O₂MT cure institutes, in order broadly to substantiate the promising individual observations made so far.

O₂ deficiency of the ear. O₂ deficiency is also frequently the primary cause of *severe hearing defects*. A well-known example of this is the *Ménière's disease* [415] which, if it occurs repeatedly, often leads to a loss of hearing in the right ear. A Ménière attack, which is characterized by severe labyrinthine vertigo which does not usually subside for several hours, is often triggered when hypotensives experience phases with particularly low blood pressure and (or) O₂ status. We already have experience of

the successful combat of Ménière attacks with the O₂MT, although only in a small number of patients. The O₂MT can only contribute little to the direct alleviation of the distressing giddiness, which frequently leads to collapse. Nevertheless, its application in the acute phase is called for in order to reduce the risk connected with the collapse, reduce the impaired hearing that occurs in this phase, and accelerate the subsidence of giddiness. The *recommended therapy of Ménière's disease* consists in using the 80 min O₂MT nicotinic acid procedure, KA 1 variant (cf. Table 32) to treat patients with signs of regulatorily conditioned hypertension or with arteriosclerosis, during a period of relative well-being. After one or two treatments the O₂ status is generally only raised slightly, but the blood pressure and the circulatory conditions are improved to the extent that, according to individual experiences so far, the frequency of the Ménière attacks is greatly reduced, or even ceases altogether. It would be a good thing if the observed effects of this concrete therapy [106] (see Paragraph 5.2.3) were at last confirmed and utilized in the specialist clinics responsible.

5.3.5 Liver, stomach and intestines

It is known that arteriosclerosis of the hepatic artery or following vessel branches, or the O₂ deficiency hereby caused lead to *liver atrophy*. The pathologist then speaks of a hard, arteriopathic liver. In accordance with Paragraph 5.2.2 it should be possible to alleviate or avoid liver diseases of this origin by treatments undertaken early enough against the drop in the O₂ status and against arteriosclerosis. There are reports in [10] of significant curative effects by means of exercise training in *subsiding hepatitis, fatty liver and liver diseases* (including late consequences of liver cirrhosis). It is therefore not surprising that variants of the O₂MT can offer even more effective help, as this therapy can be begun in early stages.

An application of the O₂MT seems to be particularly indicated in *chronic progredient hepatitis*, according to the results of an outpatient treatment compiled in Fig. 257. In this way the PO_{2-art} of such a patient could first be raised from 74 to 102 mmHg (9.9–13.6 kPa). Unfortunately a virus infection, lasting approximately 17 days occurred just 18 days after this cure period, which immediately made the PO_{2-art} drop back to 75 mmHg (10 kPa). Despite this disturbance, the great improvement in the transaminases, shown in the figure below,

The very frequently observed *impairment of hearing in older age* correlates with the drop in cardiopulmonary performance. In order to delay the onset of this impaired hearing, the O₂MT procedure should be applied prophylactically between the ages of 50 and 60, e.g. in accordance with the variants and recommendations given in Paragraph 4.2 [421]. It must always be remembered here that irreversible damage once occurred can never be eliminated.

The *therapy of the sudden loss of hearing* should be begun within 3–4 days after the onset of the event. Pioneering positive experiences using the hyperbaric oxygen chamber have been gained by Fischer in Nordrach-Klausenbach (FRG) with large numbers of patients [416]. Reference [417] contains reports of good success of inhalation therapy with a mixture of 95% O₂ and 5% CO₂. Good results have been gained with the 15 min O₂MT quick procedure, GK 2-I variant, in our Institute and by Axmann (Hoyerswerda, GDR). The hyperbaric O₂MT quick procedure, GK 7 variant, is particularly indicated for this task of therapy.

was observed. Whether the improvements in the O₂ status observed in this example were sufficient to transform the changes in liver tissue definitively from negative to positive, could not be recognized, due to too short an observation time. It is very probable, however, that *the triggering of new attacks and hence the progredience of the complaint* can be alleviated if an increased level of the O₂ status, or of η , exists permanently before infections and if, during infection, the therapy is immediately performed (shortening of the period of convalescence). Since then the renormalization of the transaminases has been observed in 3 further cases; also good effects in the combat of liver cirrhosis. However, there were also cases with chronically aggressive hepatitis, in which no reduction in the levels of transaminases were found. Such negative findings are a challenge to undertake further attempts using the intensive variants of the O₂MT, given in Paragraph 4.2 (e.g. GK 4-II, GK 4-III, GK 7).

This, too, is a very fertile field which urgently requires further clarification by clinical research with large numbers of patients.

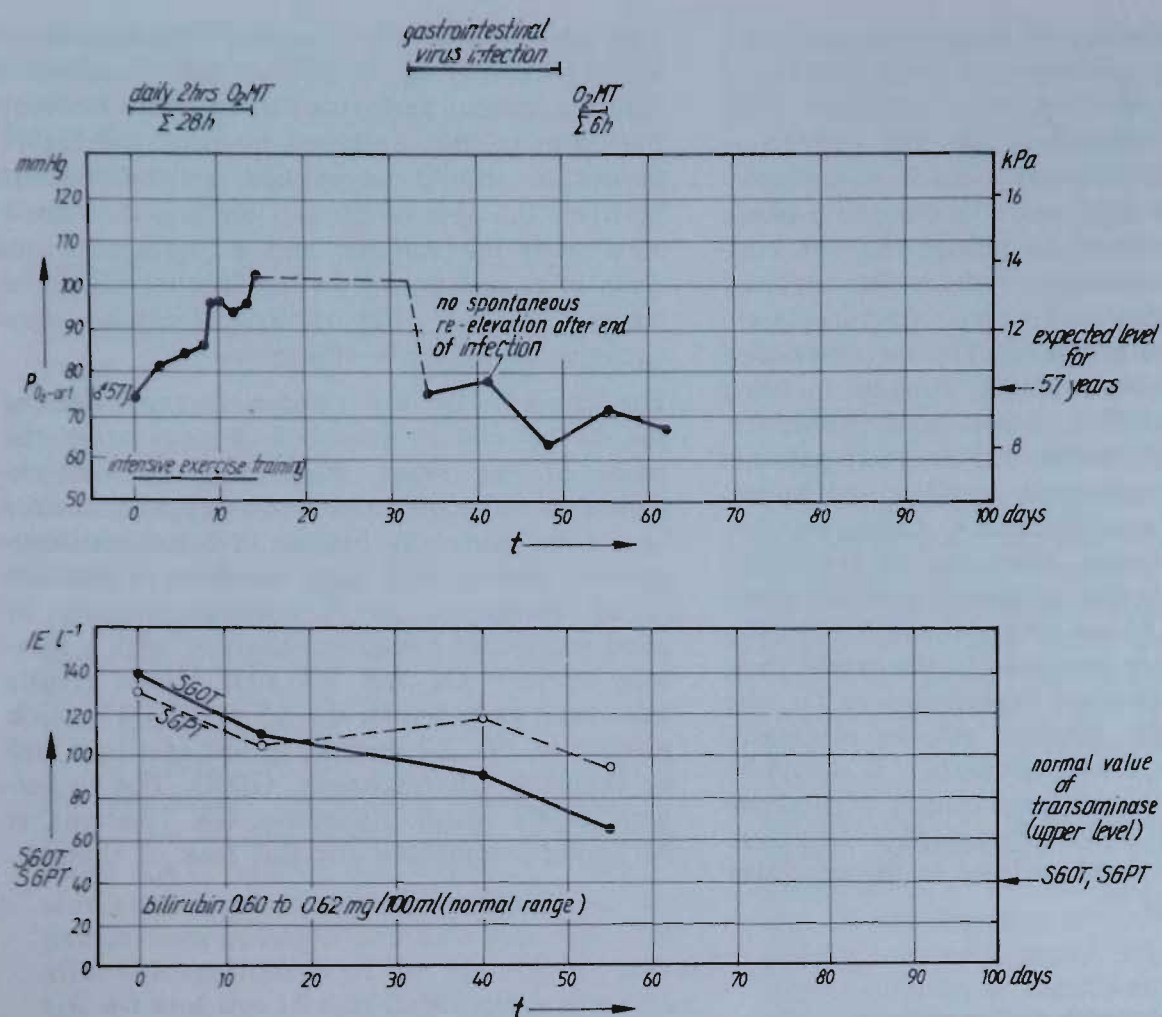


Fig. 257 Change in the arterial P_{O_2} (above) and improvement in the transaminase levels (below) by the ambulant O_2MT treatment (variant GK 4-I, 2 h per day) of a patient with progredient chronic hepatitis. Initially positive treatment interrupted by virus infection

5.3.6 Kidney

The O_2MT should be able to help in the kidney area, particularly by means of its antiarteriosclerotic components. It is known that repeated long-term periods of hypertension regularly lead to *arteriosclerotic alterations in the kidney*. The vasa afferentia are the most affected, the lumen being increasingly constricted by the incorporation of mesenchyme in the vessel wall. Secondly, the glomeruli sclerose and the affiliated renal tubuli atrophy. The mentioned constriction of the lumen soon leads to a drop in circulation of the kidney. As this procedure progresses the amount of filtrate gradually falls with the increasing failure of the glomeruli, and the blood flow of the kidney deteriorates further. Thus a feedback system presents itself, in which the reduction in renal circulation and the atrophy of the parenchyme in turn lead to hypertension, or intensify it.

This feedback mechanism should mean that the *affected kidney contributes to the fixation of hypertension*. If this process is very pronounced, it results in cirrhosis of the kidney. These specific connections endow the early combat of irreversible degeneration of arterial branches and arterioles in the vascular kidney with particular importance. Due to the feedback mechanism mentioned, the analysis of the kidney function is a good indicator of the stage of the hypertension.

In relative rare cases disorders of the kidney function are the primary cause of hypertension. Clinical experience with the prophylactic and therapeutic application of O_2MT indicate that the probability of kidney damage caused by incoming toxins can be considerably reduced if the O_2 status is maintained at a high level, over long periods of time with few interruptions.

5.3.7 Pancreas

It is known that the proteohormone insulin is formed in the β -cells of the islets of Langerhans in the pancreas, a process that is apparently very sensitive to O_2 deficiency. This can be concluded from the increase in the frequency of diabetes mellitus with advancing age, which roughly correlates with the drop in cardio-pulmonary performance, or in the O_2 uptake, at rest. However, in senile diabetes the average O_2 metabolism does not drop below the conservation metabolism, for the decline in insulin production is of reversible character in the first few years after the onset of senile diabetes at least. Thus it has been known for improvements in senile diabetes to occur with the transitions to a changed lifestyle with energy-demanding exercise training. A very significant drop in post-therapy blood sugar levels could almost always be observed in senile diabetics after the

O_2MT (partly influenced by more effective glucose catabolism). The improvement was often so great that just a light diet was enough to keep the blood sugar sufficiently low. Several cases have been reported to us in Dresden of insulin-dependent diabetics between the ages of 50–70 years, who had to reduce their insulin dose significantly after O_2MT in order to avoid hypoglycemic episodes. In one case (reported by Skeiner, Puch, Austria) the patient could switch to oral antidiabetics and finally come off these too.

In several cases with so-called chronic pancreatitis a normalization of the amylase levels in blood was observed after the procedure. Strict fasting with the breakdown of protein stores [233] also causes a decline in senile diabetes (cf. Fig. 265), a further indication of the synergistic effect of fasting.

5.3.8 Myocardium

In the *myocardium* there are specific conditions for the supply of O_2 (cf. also Fig. 93 above). The normal mean PO_{2-ven} is approximately 17 mmHg (2.3 kPa). Circulation and O_2 consumption are not constant. The temporal course of the mean PO_2 in the heart muscle during hard physical labor is shown in Fig. 258, on the basis of calculations by Thews. In the systole the circulation in the inner layers of the

left ventricle temporarily stops completely, for mechanical-vascular reasons. The integral PO_2 here has the lowest level of all healthy tissue in the organism. On the other hand, the systole has the highest O_2 consumption. The inner layers of the left ventricle are therefore the area most threatened by oxygen deficiency.

The myocardium, with the combat of its insufficiencies and diseases, is one of the main

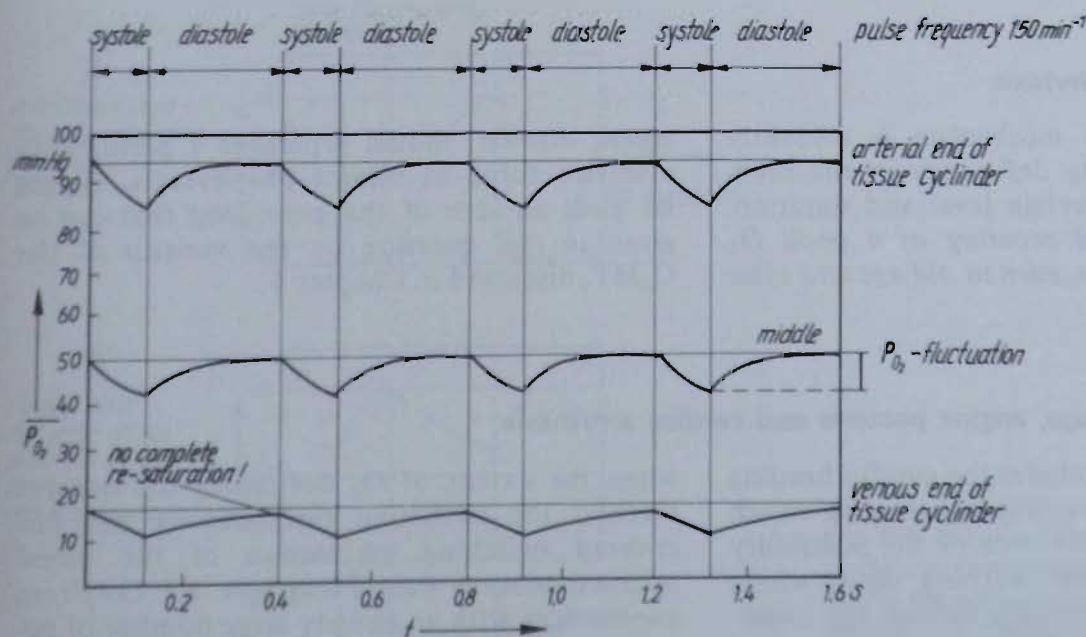


Fig. 258 Temporal change in the mean PO_2 of the heart muscle in three different areas of the tissue cylinder during heavy physical labour; modified according to G. Thews [420]; 1 mmHg = $1.33 \cdot 10^2$ Pa

domains of O_2 MT research. This is partly a consequence of the fact that the results of our work on the development of the cancer multistep therapy, with its selective triggering of irreversible hemostasis in the cancer tissue, also helps, or can also help, in the combat of the myocardial infarction because the same mechanism of vascular occlusion is brought about here as occurs naturally during the infarction [366]. Various results, immediately utilizable for the patients, are now open to cardiologists: they range from prevention, through prophylaxis and therapy, to rehabilitation. It is now vital that the responsible medical practitioners read — with great sobriety and objectivity — the original papers, partially co-authored with Reitnauer [e.g. 111, 122, 146, 148, 150, 171, 198, 199, 338, 366] and also the sections of this book dealing with this subject. It is composed of measured results, experi-

mental findings, clinical experiences, methodological studies but also of speculative ideas and working hypotheses of our small Dresden research group, all of which are in need of verification, confirmation and comprehension. In this time of a flood of information, the gaining of many active cohelpers and cochampions, not only within the group of friends of the "Gesellschaft für Infarktbekämpfung" in Schorndorf-Haubersbronn (FRG) is necessary for the further success of our movement. The author relies here on the younger generation, who have the mental energy, despite the daily hectic pace in hospitals, to become accustomed to thought processes which cannot, or cannot yet, be found in official textbooks. The following paragraphs aim to give a survey of our conclusions from our own work and from sports medicine, which is close to us, under the aspect of making them quickly utilizable for the patient.

5.3.8.1 Infarct prevention

We can expect a great contribution to *infarct prevention* and to the prevention of respective prestages such as angina pectoris, arrhythmias and other cardiac insufficiencies of varying kinds, *from a prophylaxis of arteriosclerosis*. We have already explained elsewhere (see Paragraphs 3.4.4, 5.2.1, Figs 212 and 243) our idea that arteriosclerotic degeneration of the arterial vessel wall can be delayed if, by using the O_2 MT, the resting PO_{2-art} is maintained as continuously as possible at levels above 75–80 mmHg (10–10.7 kPa) from the age of 60–70

years onwards. The transcutaneous PO_2 measurement after blood compression and release in a volunteer who had used the O_2 MT for 15 years, shown in Fig. 212 A, is a first indication that a prophylaxis of arteriosclerosis succeeds, or can succeed, in this concrete way.

A further contribution to infarct prevention arises from sports medicine, by which the drop in COP with advancing age (cf. Figs 66, 68 and 153) is countered by *daily exercise training* (e.g. 10 min minimal training with raising of pulse rate to 180 – age, see Paragraph 1.1.9.5).

5.3.8.2 Infarct prophylaxis

Since the infarction mechanism is evidently released when the O_2 deficiency in the myocardium exceeds a certain level and duration, *the maintenance and securing of a good O_2 status with few lapses, even in old age and after*

severe distress, should represent a particularly effective form of infarct prophylaxis. Figure 66 gives an idea of the great help that can be given in this question by the variants of the O_2 MT, discussed in Chapter 4.

5.3.8.3 Preinfarct stage, angina pectoris and cardiac arrhythmia

Infarct prophylaxis includes the careful heeding and combat of the warning signals with which Nature generally gives notice of the possibility of an infarction. These warning signs, which must be taken very seriously, include the occurrence of cardiac arrhythmias and, most importantly, attacks of *angina pectoris*. According to our concept, angina pectoris attacks occur

when the extent of O_2 deficiency has not yet reached the switching threshold of our discovered switching mechanism of the blood microcirculation (see Paragraph 1.1.1). From experiences with an already large number of patients with cardiac insufficiency we can state with certainty that, in a very high percentage of cases, angina pectoris complaints and also the

occurrence of cardiac arrhythmias are repressed in terms of frequency and severity, if not even eliminated, by O_2MT variants adapted to the individual case. Cases have been reported of heart patients who were faced with the prospect of bypass operations, but who first underwent an O_2MT procedure. All cardiac complaints and also ECG anomalies disappeared. They could be spared the operation. A large number of findings were observed or reported in which cardially conditioned breathing difficulties or anginal complaints disappeared in physical exertion.

A further, simultaneous method of combatting angina pectoris is either the application of a stomach-resistant strophanthin preparation (Strodival mr) on the basis of a cure or the *ad*

hoc application of the *Strodival special preparation*, developed in conjunction with the author, dealt with in more detail in the following paragraph. Dohrmann [147] reports on the arrest of angina pectoris attacks in 85 % of cases within approximately 8 min after the perlingual administration of this preparation.

There are reports on an extensive reduction of deaths due to infarction in underground mining by means of immediate treatment with perlingually administered g-strophanthin (e.g. Strodival special) in anginal complaints [421]. Under otherwise identical conditions and with roughly the same number of heart attacks (around 250), 11 deaths occurred without immediate Strodival therapy, and none with this prophylaxis.

5.3.8.4 Infarct mechanism

Primarily as a result of Reitnauer's experimental skill we have gained deep insight into pathophysiological processes of the myocardial infarction and its combat, from micro pH measurements on pulsating rat hearts (cf. Fig. 105) with artificial triggering of infarct (cf. Fig. 106), with controlled termination of the O_2 -deficient phase (cf. Fig. 107) and with administration of g-strophanthin (cf. Fig. 84). Further decisive aspects of the mechanism ensued from several years of our research into the details in the selective triggering of hemostasis in the cancer

tissue by optimized over-acidification of the tissue plus synergistically acting hyperthermia.

On the basis of the well-known processes in the myocardium, described in Figs 258 and 259, our insights were particularly deepened by the pH measurements in the myocardium (Fig. 260), the analysis of the consequences of the drop in pH occurring in the O_2 -deficient infarcted volumes, in accordance with Table 39, and the survey of main influences, compiled in Table 40. The pH measurements in Figs 84 and 107, and the measurements of P_{O_2} and micro-

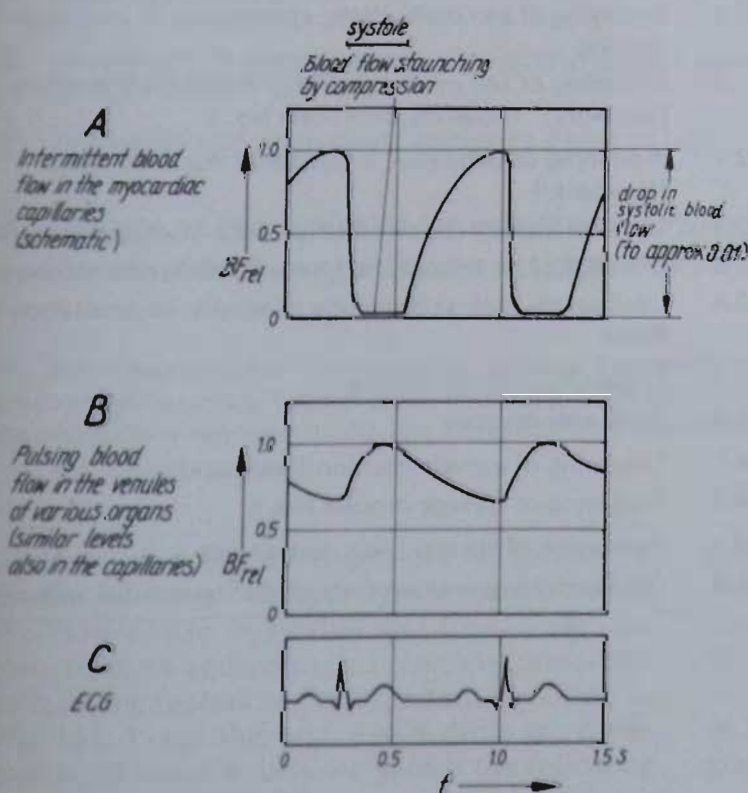


Fig. 259 Periodic blood flow reduction, due to vascular compression in the myocardium during the systole of approximately 0.3 s duration. (A). The specific hemodynamics renders the myocardium greatly sensitive towards triggering of stases, compared with other organs (B).

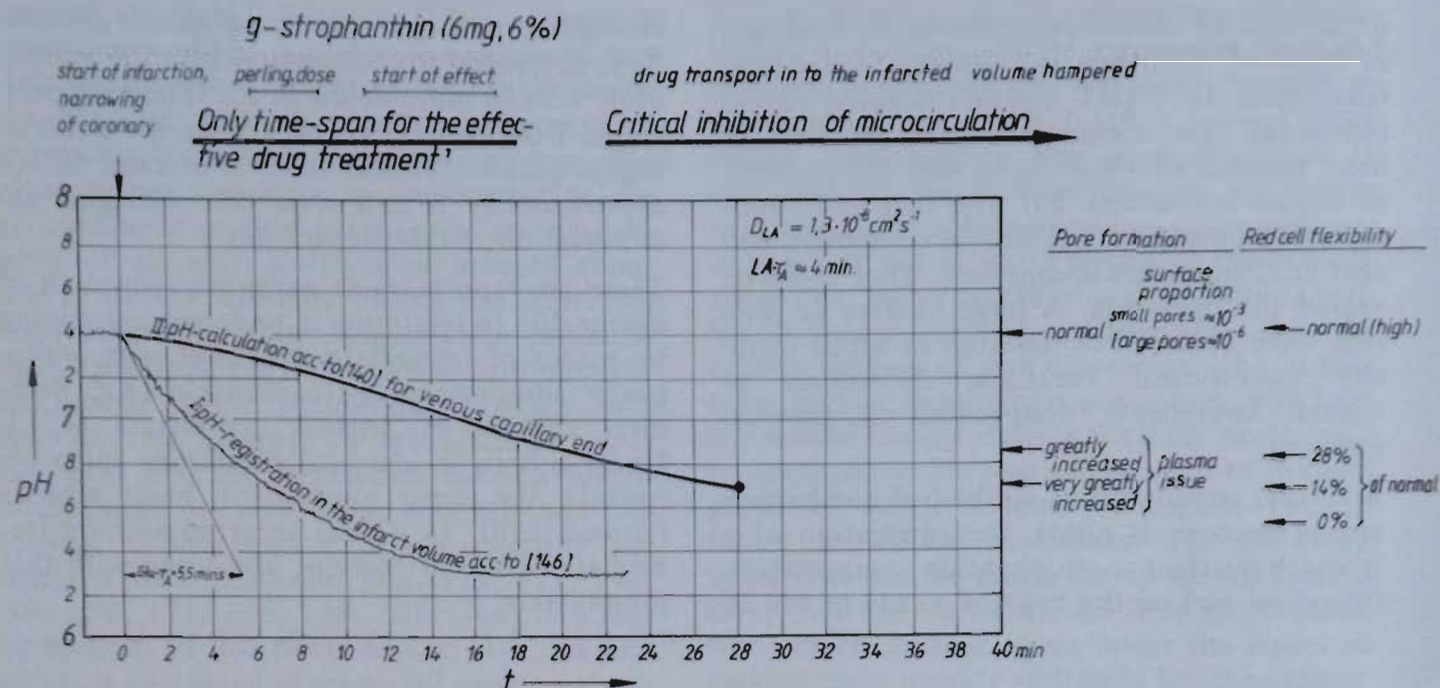


Fig. 260 Due to the soon occurring microcirculation inhibition the "effective" administration of drugs against the myocardial infarct is only possible in its initial phase (≤ 20 min)! pH-registration in an O_2 deficient volume of the myocardium after the triggering of an experimental cardiac infarct in a rat (I), and the pH course at the venous end of the capillaries in the infarcted volume (II), calculated from the registration. The time constants used for glucose-lactic acid exchange ($Glu-\tau_{\alpha}$), lactic acid drainage ($LA-\tau_{\alpha}$), and the diffusion coefficient (D_{LA}) are given in the diagram

¹ This decisive time-span is usually already up by the time the doctor or ambulance arrives. Therefore only drugs which the patient (advised by the doctor) can give himself are useful

Table 39 The multifarious consequences of the pH reduction detectable in the O_2 deficient infarcted myocardial tissue

Triggered process	Consequences
1 Structural rearrangement of cell membranes (pH 7.4 $\rightarrow$ 6.5)	1.1 Labilizing of cell membranes, stimulation of intravascular clotting 1.2 Stiffening of cell membranes (e.g. reduced erythrocyte flexibility). Triggering of process No. 2
2 Reduction in blood microcirculation	2.1 Worsening of deficiency situation of the body tissue (feedback!) 2.2 Uptake (absorption, distribution etc.) of drugs hampered 2.3 Drainage of lactic acid and lysosomal enzymes hampered 2.4 Leukocytes stick at beginning of venule; accumulation in tissue
3 Intracellular release of lysosomal enzymes	3.1 Triggering of autolysis 3.2 Small-area necrosis
4 Activation of released lysosomal enzymes	4.1 Triggering of a chain reaction (feedback) 4.2 Triggering of leakage process No. 5
5 Damage to capillaries (in lasting severe overacidification of the tissue)	5.1 Formation of edemas; wall destruction 5.2 Confluent large-area necrosis of the myocardial infarction

Table 40 Main factors influencing the pH reduction in the O_2 deficient volume of a myocardial infarction

Main factor	Comments
1. Degree of the O_2 utilization deficit in the myocardium	
2. Duration of the O_2 utilization deficit	Minimum duration for triggering infarction is dependent on influences 1, 2, 3 and 4 (e.g. 10–30 min)
3. Volume of tissue with utilization deficiency	Minimum volume for triggering infarction $v = 10 \text{ mm}^3$ (lactic acid drainage; confluence)
4. Blood glucose concentration	More severe pH reduction in diabetics with above-normal glucose level
5. Co-use of formed lactic acid as an energy substrate	Metabolized proportion increased through g-strophanthin (rise in pH)

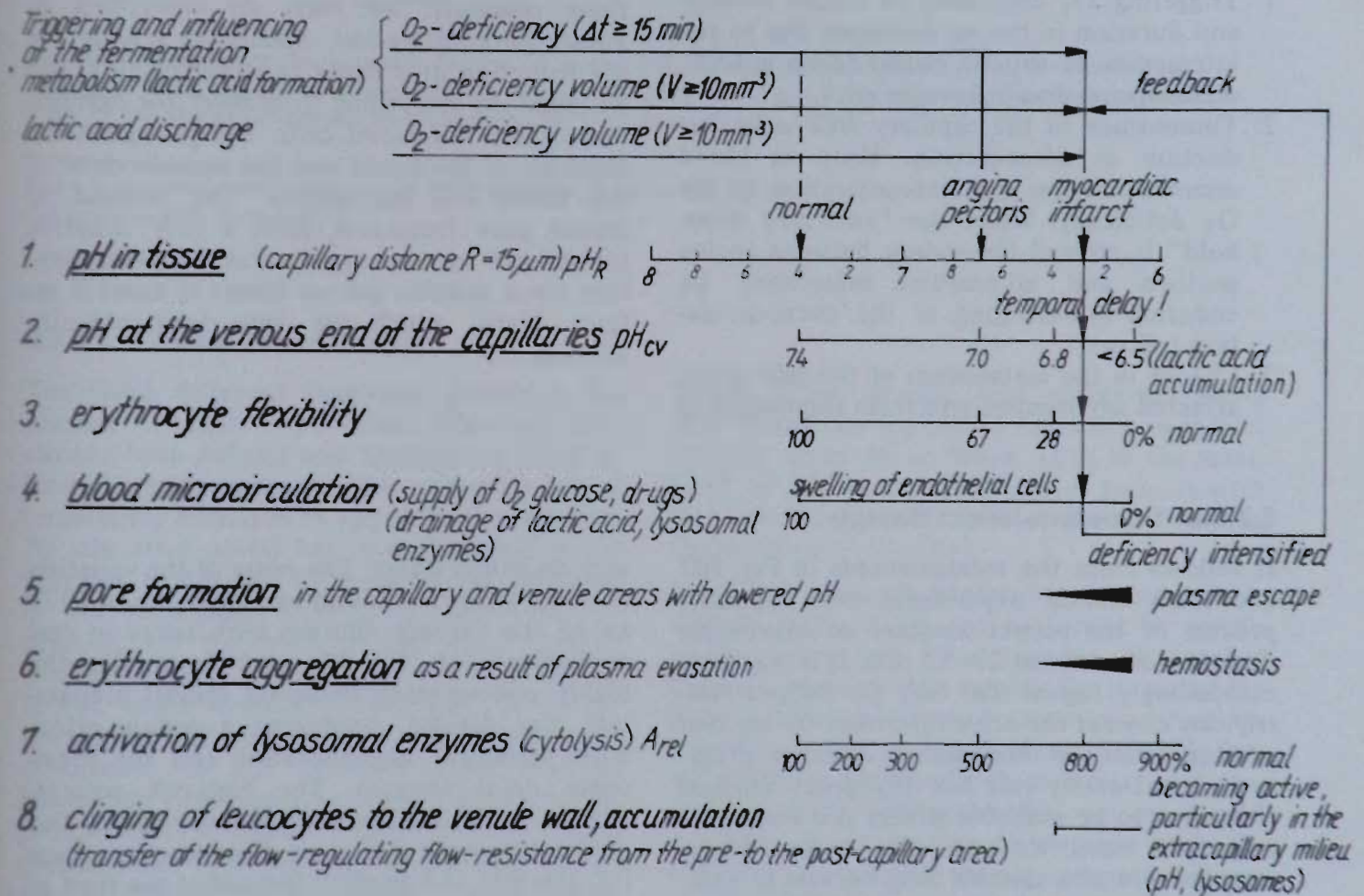


Fig. 261 Presentation of the correlation between the reduction in the tissue pH (1), the capillary pH (2), the erythrocyte flexibility (3), the blood microcirculation (4), the pore formation accompanied by plasma escape (5), the erythrocyte aggregation (6), the activation of lysosomal enzymes (7) and the clinging of the leucocytes (8)

circulation in Fig. 85 finally led us to the following concrete concepts of the mechanism of the myocardial infarction and its combat: the time relation and course of the most important influencing factors in the infarction are shown in Fig. 261. From this and, partly, from as yet unpublished latest results we gained the following

concept of the myocardial infarction mechanism: as soon as the extent of the O_2 deficiency in the affected area of the heart muscle drops below a certain critical level, the threshold of the capillary wall switching mechanism of the blood microcirculation, outlined in Paragraph 1.1.1 by means of Figs 1 and 2, is crossed

(turning-down). The metabolism of the heart muscle cells changes to fermentation and the pH situation in the affected myocardial tissue deteriorates within a few minutes, as shown in Fig. 260. The rapid drop in pH results, as we found, in the *formation of pores* near the venous end of the capillaries in the walls of these fine vessels. Plasma flows out through the pores, as shown in Fig. 75, and this leads to *jamming of red blood cells* in that area and their *aggregation*, followed consequently by vascular occlusion.

According to this, the *pathophysiological process in the myocardial infarction* occurs in the following order:

1. Triggering. O₂ deficiency of certain severity and duration in the myocardium due to the interaction of various causes (drop in COP, distress, circadian influences etc.).
2. Tumescence of the capillary wall cells. Reduction in cross-section. Drop in blood microcirculation with intensification of the O₂ deficiency. When the "switching threshold" is crossed (boundary between angina pectoris and myocardial infarction), an enduring low-charging of the microcirculation follows.
3. Change in the metabolism of the cells in the affected myocardial area from respiration to

fermentation. Drop in pH at the venous end of the capillaries (to approximately 6.7) and in the tissue (to approximately 6.0–6.3) in this area (reversible in the first 20 min).

4. Great and rapid increase in "pore formation" in the capillary wall zones with reduced pH. Plasma escape. Rise in the effective local hematocrit (reversible).
5. Retardation of blood flow. Drop in shear stress. Increase in the apparent blood viscosity (reversible).
6. Strong aggregation of red blood cells with increased hematocrit and reduced shear stress. Vascular occlusion. Hemostasis (irreversible).

New aspects of infarction therapy arise from these concepts: *we must do everything to hinder pore formation*, mainly to *reverse the pH reduction as a cause* (g-strophanthin), and we must do everything to *combat the aggregation of the red blood cells*. See [422] for the rheology of the blood and the measurement of red blood cell aggregation. The demand to hinder pore formation gives a very concrete foundation for the application of g-strophanthin (in a suitable galenic form) to combat infarct death, which we have long urgently advised.

5.3.8.5 Immediate infarct therapy

It follows from the measurements in Fig. 107 and from clinical experiences that the basic process of the infarct assumes an irreversible character after about 20–25 min. It is therefore compellingly logical that *only the patient himself can combat the acute infarction by the oral administration of immediately effective drugs*, as it is extremely rare for emergency medical treatment to be available within this very short period of time. We were able to confirm g-strophanthin as a suitable drug because it leads, within just a few minutes, to an increase in pH in the affected myocardial tissue (cf. Fig. 84), to the closure of the pores that have been formed, it leads to a rapid restoration in the tissue P_{O_2} and also reverses the inhibition in blood microcirculation that has occurred (cf. Fig. 85). Unfortunately this substance was discredited for oral administration because of its

very uncertain effect. The cause of the variation in effect [150] was found by Lippmann in 1974 to be the varying dilution with saliva in oral application (cf. Fig. 86) and from this the highly concentrated Strodival special preparation was derived, producing a certain effect with perlingual administration (on the previously dried tongue). The high-risk patient, advised by his doctor, should always carry this preparation with him in an **emergency package** (cf. Fig. 87) and apply it himself at the start of an infarction. This would not harm the patient if he made a false diagnosis. There have been several cases of patients equipped with the emergency package experiencing the prestage of a myocardial infarction with its known severe symptoms, administering the named preparation themselves perlingually and being free of all infarct symptoms after 10 min.

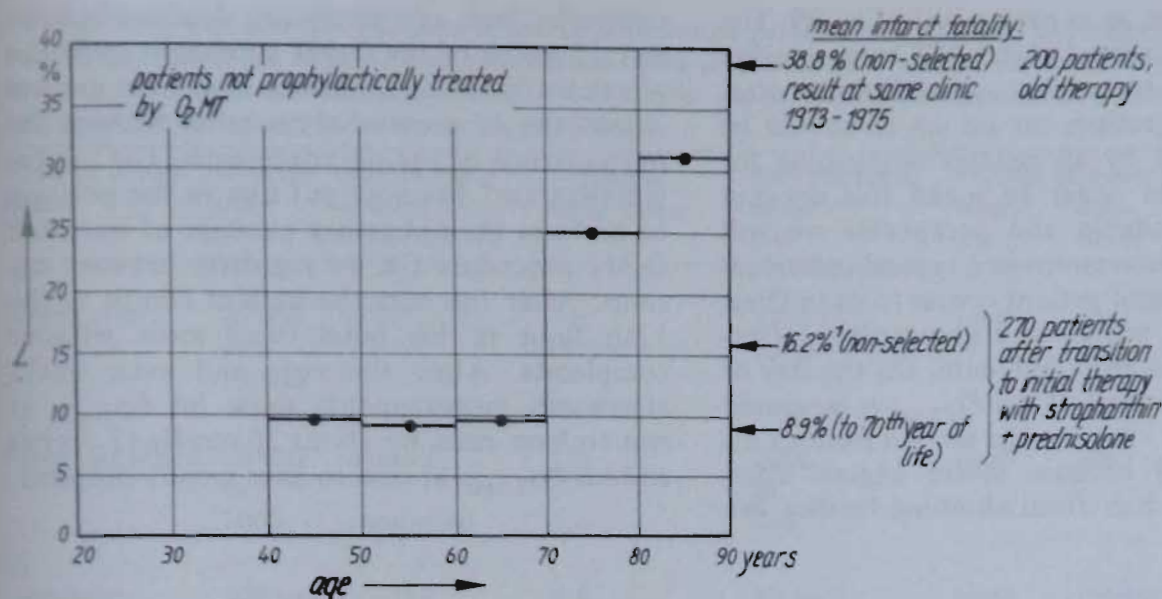


Fig. 262 Indication of the increasing fatality of cardiac infarcts with decreasing arterial PO_2 (increasing age). Results of initial therapy of infarct patients with the combination of g-strophanthin + prednisolone suggested in [144], in the Waldkrankenhaus Berlin-Spandau (R. E. Dohrmann et al. [152])

¹ In a multicentric WHO study with 7738 patients (Europe, old therapy) the mean fatality of infarcts for 1977 was given as 40% (non-selected)

5.3.8.6 Clinical infarct therapy

The three different treatment phases in the combat of acute myocardial infarction have already been defined and described in Table 8. Immediate therapy in the reversible phase (emergency situation in approximately the first 20 min after onset) has been discussed in the previous paragraph. With therapy in the clinic in the subsequent irreversible phase we distinguish, on the basis of Fig. 116, between clinical therapy *before* occurrence of the cytolytic chain reaction (time-span 20 to approximately 120 min) and clinical therapy *after* occurrence of the cytolytic chain reaction (time-span from approximately 120 min to approximately 2 days). High dosage α -methyl prednisolone (von Ardenne and Kern [144]) is used to inhibit the lysosomal cytolytic chain reaction by stabilizing the lysosomal mem-

branes. It has already been mentioned above that Dohrmann achieved a reduction in infarct lethality from 38 to below 16% in the treatment of 270 nonselected infarct patients with this combination in his clinic in Spandau (Berlin West) [152, 153].

If the infarction mechanism has entered its irreversible stage, which can no longer be significantly influenced, the *chances of survival depend greatly on the current O_2 status of the patient*. This is indicated by the clinical findings analysed in Fig. 262, according to [152]. Persons with an increased risk of infarct (old age, warning signs, unfavorable PO_2 values) should therefore do everything to improve their O_2 status as much as possible by adapted variants of the O_2 MT.

5.3.8.7 Infarct rehabilitation

A considerable increase in the patient's capacity for exercise occurs even during implementation of the 36 h (18 day) O_2 MT procedure GK 4-I, in correlation with the rise in the arteriovenous PO_2 difference measured without O_2 inhalation. This rapid increase in capacity for exercise is of great significance for rehabilitation after a myocardial infarction, where the treatment has

so far trodden a tightrope between the triggering of a further infarct with too much exertion and the unnecessarily long return to a normal lifestyle, adapted to the case, with too little. This former tightrope is made very much wider and thus the patient risk significantly reduced by the "initial mobilization" of the infarct patients, occurring after the first sessions of the

O₂MT treatment, as in examples in Fig. 89. The mobilization effect of the O₂MT thus signifies a decisive aid to patient rehabilitation after myocardial infarction, an aid which should be quickly grasped by all centers responsible for this problem. In order to make this demand more understandable and acceptable we will give here the observations in a typical individual case: a middle-aged patient comes to us in Dresden soon after suffering a myocardial infarction, to undergo an O₂MT cure. On the day of his arrival a low level of the $P_{O_2\text{-art}}$ is measured and he can only climb to the second floor of his 13-storey hotel because severe anginal complaints prevent him from climbing further. We

categorize him as "physically disabled". After just 12 hours of the O₂MT treatment cycle this physical disability vanishes and the patient climbs the 13 storeys of his hotel without the reoccurrence of anginal complaints. The "initial mobilization" has now put him in the position to perform the obligatory exercise of our 36 h O₂MT procedure GK 4-I regularly between sessions. After the cure the patient climbs to the 13th floor of his hotel twice more without complaints. After the cure and even weeks afterwards measurements show his $P_{O_2\text{-art}}$, at rest to have risen by about 20 mmHg (2.7 kPa) and his $P_{O_2\text{-ven}}$, at rest, to have greatly dropped.

5.3.9 Vascular system. Fasting as a further step of therapy

The arterial side of the blood vessel system, on whose functioning ability so much depends for human health and life, is a main target area of the O₂MT. The various types of blood vessels and some of their data are compiled in Table 41. The most important disease of the blood vessel system, arteriosclerosis, and therapeutic

measures to combat it using O₂MT have been discussed in Paragraphs 3.4.4 and 5.2.2. We will therefore only supplement this here with a few physiological considerations.

The inter-relationships between causes and effects in the genesis of arteriosclerosis are shown schematically in Fig. 263. Sclerogenous

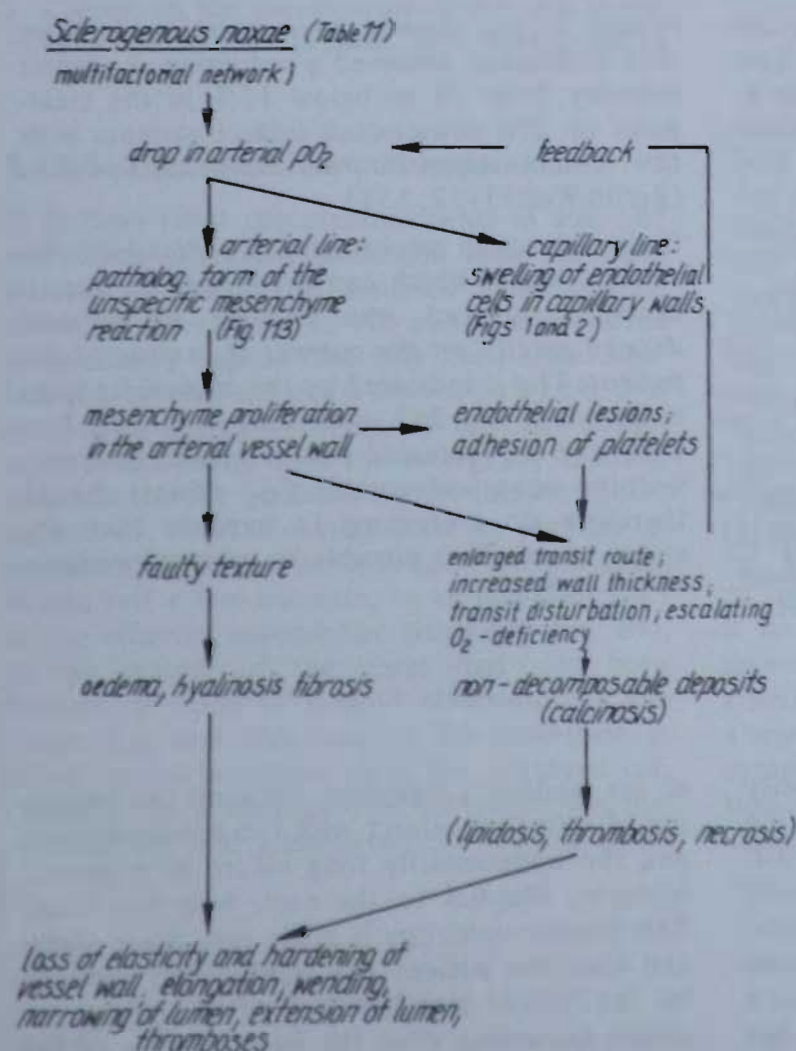


Fig. 263 Schematic presentation of the interrelationships between causes and effects in the emergence of arteriosclerosis; according to [381] with modifications

Table 41 Diameter and wall thickness as well as relationships between wall thickness and inner radius for varying contraction conditions of the smooth musculature in the different vessel types of the human organism. By aggregation and attachment of platelets at injured sites of arterial vessels, a critical increase of the "effective wall thickness" can occur, which is decisive for regular supply [383]

Type of blood vessel	$\varnothing$ range μm	Vasomotor activity	Thickness inner radius	Wall thickness range μm	Portion of major components endo-thel.	elast. fibres	muscle fibres	collag. fibres
1. elastic artery	20 000 to 10 000	—	1:6 (1:5 to 1:7)	3300 to 1700	small	very big	medium	big
2. muscular artery	10 000 to 1000	relaxed contracted	1:5 1:3	2000 to 330	small	big	big	medium
3. arteriole	200 to 20	relaxed contracted	1:5 1:1	40 to 20	small	medium	very big	medium
4. capillary	7 to 5	—	1:2.5 (1:5 to 1:10)	0.7 to 0.9 (to 2.5 in diabetic protein depositing)	very big	nil	nil	very small
5. venule	20 to 500	relaxed contracted	1:12.5 (1:10 to 1:15) 1:8.5 (1:7 to 1:10)	1.6 to 40	small	small	big	small
6. medium vein	1500 to 15 000	relaxed contracted	1:12.5 (1:10 to 1:15) 1:8.5 (1:7 to 1:10)	120 to 1800	small	medium	big	medium
7. large vein	15 000 to 30 000	—	1:12.5 (1:10 to 1:15)	1200 to 2400	small	medium	medium	very big

noxae, of which O_2 deficiency is one — or, rather, which cause nearly all O_2 deficiency (see measurements in Paragraphs 1.1.8.3 and 1.1.9.3) — trigger the swelling of endothelial cells in the capillaries, thus reducing their cross-section, and also the initially reversible incorporation of mesenchyme in the arterial vessel walls. An increase in peripheral resistance is observed here as the direct response. The incorporation of mesenchyme into the arterial vessel walls, which is based on the unspecific mesenchyme reaction [172, 194], leads in particular to thrombocytes being strongly attached [383] with critical changes in the vascular lumen and, if the changes persist, to a loss of elasticity, among other things, and also a hardening of the vessel wall as a result of deposits.

These changes are often localized at ramifications where, according to [173], *turbulences in the bloodstream* occur. These turbulences, in addition to mechanical effects (e.g. lesions), probably cause a local adherence of platelets and a reduction in the O_2 supply to the vessel wall.

It was explained above that there are probably two stable states locally in the walls of the muscular arteries and the arterioles: condition A with a small wall thickness (normal state) and condition B with critically increased wall thickness (pathological state). Paragraph 5.2.2 also discussed the fact that the intensive temporary raising of the O_2 metabolism in the critical area of the vessel wall can cause state B to change to the positive state A.

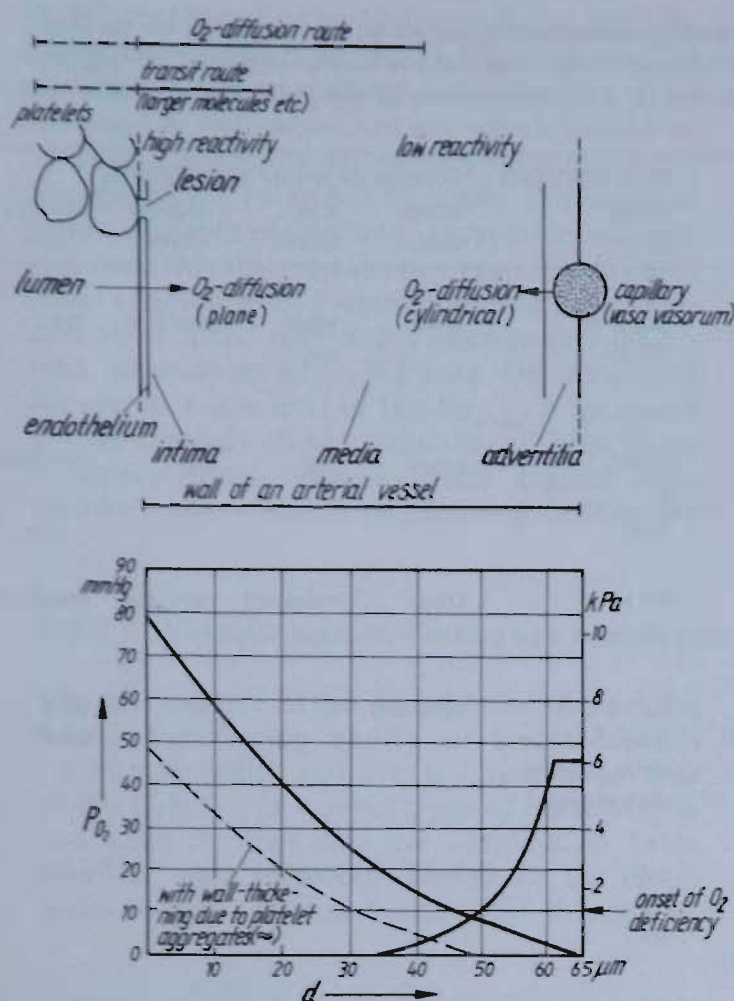


Fig. 264 O_2 supply to the arterial wall by diffusion from the lumen (plane-symmetric) and from the vasa vasorum (cylindrical-symmetric). For calculation see Fig. 243

On the subject of this change, which can last for months or years, Fig. 243 shows a quantitative presentation of the PO_2 distribution in the vessel wall under the given margins, calculated with the aid of the "diffusion equation for the case of planar interfaces". It gives exact information on how greatly the PO_{2-art} and hence also the PO_2 level in the critical wall areas of the arterial vessels, can be increased by the doubling or trebling of the O_2 proportion in the inhalation air. Like the further presentation in Fig. 264, this calculation reveals the dominant role of the O_2 diffusion (plane diffusion) from the lumen with its high PO_2 level, to the critical areas of intima and media. The calculation also shows us that the direct O_2 diffusion from the lumen is enough to supply the healthy arterioles with the greatest wall thickness ($d = 40 \mu m$) sufficiently with oxygen. But both presentations also show how greatly the O_2 supply in the critical wall areas of the arterial vessels deteriorates when local wall thickenings (adherence of platelets) occur and,

simultaneously, the resting PO_{2-art} drops, e.g. with increasing age. In order to keep the development of arteriosclerosis in the vascular system at a low level, persons over 50 should – as explained in Paragraphs 3.4.4 and 5.2.2 – do everything in their power to raise their PO_{2-art} at rest, to as high a level as possible and for as long as possible. As soon as a selected variant of the O_2MT has caused the narrowest capillary cross-section to be dilated (see Paragraph 1.1.1 and Figs 1 and 2), the peripheral resistance in the circulation and hence also the blood pressure drop immediately and lastingly (cf. Paragraph 5.2.4).

Effects on the arterial side of the blood vessel system similar to those attainable by O_2MT can be gained by the clinical implementation of a 21-day fast [350]. Details of the program of a juice fasting period in accordance with Krauss are compiled in Table 42. How strongly the therapeutic effect of fasting influences the arterialization system of the lung, for example, can be seen from this finding: in an experiment with 12 patients whose PO_{2-art} under conditions of rest was on average 72 mmHg, this resting value rose to 94 mmHg after physical-dietetic measures spread over 5 weeks. The main contribution to this increase was made by the 21-day juice fasting period as in Table 42. Like the effect of the O_2MT , the effect of fasting is multifactorial. One factor in fasting is the improvement in the Broca index, especially in overweight persons. A typical example of the improvement in this index possible by fasting can be taken from Fig. 265. In other words, after the fast there is a considerable saving in circulatory work, which is expressed in a slight drop in pulse frequency. A further important effect of fasting is the breakdown of waste products, e.g. from degenerated regions of the arterialization system of the lung and from the walls of the (arterial and capillary) vascular system. The latter effects of fasting are discussed in [369]. It is reported that the protein deposits on the capillary walls, which lead to an increase in wall whickness from approximately $0.8 \mu m$ up to $2.3 \mu m$ (only) in diabetes mellitus, disappeared after fasting. It is known that the organism, in its lack of substrates, mainly falls back on tissue components that are inessential for life, superfluous or even harmful. If we bear in mind the results of observations of the eye-ground before and after fasting, and also of the strong lipolysis that occurs during fasting and which is even intensified by a low level of physical activity [350], this justifies the expectation that fasting can also contribute to the breakdown of intra- and extracellular lipid

Table 42 Program of the 21 day juice fasting period – clinical implementation [350]

1.	Methodology of the therapeutic fast
1.1	Serving the juice in 3 meals morning fruit juice midday vegetable juice or vegetable broth evening fruit juice
1.2	When juices with low vitamin C content (apple, bilberry or grape juice) are given as main juices, the daily ration of vitamin C must be ensured by a small quantity of additional, vitamin C-rich juice (e.g. 150 ml citrus juice, 40 ml sea buckthorn juice)
1.3	In case of thirst, reduction of the concentration capacity of the kidney, increased NPN in the blood, or during a fasting crisis, the fluid intake can be increased by tea
2.	Measures in the therapeutic fast
2.1	To ensure the patient's compliance he must be informed of the purpose, chances of success and the course of the treatment. Attention drawn to the fact that sensations of hunger do not usually occur and that possibly occurring critical moods are harmless
2.2	Bowel movement on the 1st and 3rd days by means of a (preferably saline) laxative. Intestinal enema (1/4 l) at body temperature daily if at all possible but at least at intervals of 2 days
2.3	Care of heat regulation. Warm clothing, covers, partial baths at increasing temperature
2.4	Dermal and mucodermal care. Mouthwashes and brushing the tongue several times a day. Small hydrotherapeutic measures, such as skin-brushing, washes, showers, compresses
2.5.	The faster's frequently felt need for peace and quiet must be taken account of in the surroundings.
2.6	Bland and light transitional diet at the end of the fast to start up enzyme secretion and peristalsis again. Under no circumstances a sudden transition to a normal diet. Diet sheet somewhat as follows: 1st day morning one grated apple midday one plate potato or cereal soup evening two pieces of fruit (ripe) one slice crispbread with a scrape of butter (5 g) 2nd day early 100 g "Kollath breakfast" 1 piece ripe fruit midday 100 g salad, or low fibre vegetables, 150 g potatoes evening fruit, 2 slices crispbread, 15 g butter
2.7	Fasting crisis with disruption of the vegetative system (e.g., depression, headache, vascular lability or flaring-up of symptoms of illness) to be cared for by additional administering of black tea, also coffee and 20 g honey
2.8	A light sedative and antispasmodic local applications of warmth are usually enough to revive the patient's sense of well-being

deposits in the wall of arteriosclerotically altered vessels (cf. Fig. 244).

The *equidirectional effects of the O₂MT and fasting* make it obvious to combine these two mutually complementary therapies in order to gain even stronger effects, especially on the arterial side of the vascular system. For this reason a period of juice-fasting was named as a further step in combination with the 36 h O₂MT variant GK 4-I. This must be clinically implemented, despite the extra cost and time involved.

Nature has adapted the vascular system to the high cardiopulmonary performance of youth and middle age. When increasing age leads to a

drop in performance of the cardiopulmonary system and hence in the O₂ uptake, at rest, this adaptation deteriorates and arteriosclerotic damage looms. This damage is by no means evenly distributed over the whole of the arterial side, but is known to manifest itself with greatly increased probability at certain sites of the arterial network, e.g. at ramifications and endothelial lesions. Which area and which organ connected to it are first affected in the individual case depends on the chance nature of the vessel wall architecture (Fig. 264, vasa vasorum).

The localization of the pathological alteration in the arterial wall is largely decisive for the optimal design of the 3rd step of the O₂MT

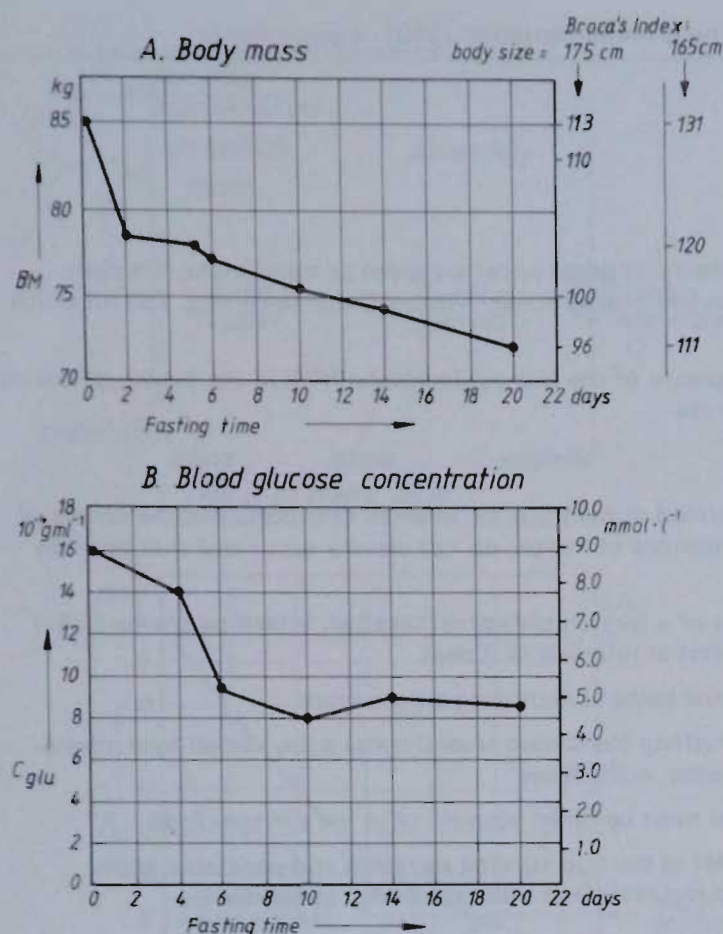


Fig. 265 Reduction in body mass or of the Broca's Index (A) and the fasting blood glucose concentration in a diabetic during a 21-day fasting period [350]

variant applied. The localization determines in each case the measures to increase circulation during the application of therapy (see Paragraph 2.3.5).

Arteriosclerotic or capillary vascular damage is often such that (first) the *blood supply of the extremities is impaired* [423]. In 70% of cases of this type coronary sclerosis occurs simultaneously [424]. Usually the peripheral arteriosclerosis or capillary constriction even precedes the coronary sclerosis. The first signs of weak circulation in the extremities (e.g. the onset of intermittent claudication) should always be taken very seriously and seen as ground for early therapeutic measures. We must never wait until there are signs that severe irreversible tissue damage (e.g. pregangrenous conditions), caused by O_2 or supply deficiency, have been triggered. That the permanent restoration of the O_2 status and of the COP, which declines with age, can lead to a decisive improvement of the situation is shown by the following case: in an older patient with so-called "smoker's leg" the pregangrenous situation was so advanced that the doctor ordered amputation within 14 days. The patient used this time for the im-

plementation of the 36 h O_2 MT procedure GK 4-I (cf. Table 27). He then presented himself for amputation in the clinic but the same doctor declared after examining the leg that amputation was no longer necessary. Amputation could also be avoided in several similar cases of this type. This is a particularly fruitful area of indications of the O_2 MT.

In accordance with Chapter 4 the variants GK 2-I, GK 4-III and GK 7 with their measures in the 3rd step for the *improvement of the flow properties of the blood* by means of hemodilution [47, 114] are indicated for circulatory disorders in the extremities or certain organs. We would emphatically refer the reader here to the hemorheological papers [425, 426], the infusion of *buflo-medil* (Bufedil), and the oral administration of *pentoxifyllin* [427].

In experiments of this type measurements of the mean tissue PO_2 (and the tissue temperature) behind the arterial or capillary constriction enabled us to pursue the O_2 situation before, during and after the therapy procedure, and hence gain *numerical data for the success of therapy* in the individual case.

A 51-year-old patient could be spared a bypass operation on the heart by means of the O_2 MT variant GK 4-III (plus 4 HOT* treatments). Because of a poor exercise ECG, coronary angiography had been performed. It revealed a severe affection of the three coronary arteries. In the course of treatment η was raised from the critically low level of 13% to a lasting level of 31%. The cardiac complaints which had previously occurred even in minimal exertion did not take place. It is also possible to alleviate arteriosclerotic constrictions by the combination of O_2 MT with EDTA (ethylene diamine tetraacetic acid) treatment; dose 3 g in a 50 ml infusion solution, supplemented by magnesium, vitamin B_6 and others; 20 treatments of 3–4 h twice a week (decomposition of deposits in the arterial walls).

Finally, we would remind the reader of the non-invasive method of transcutaneously measuring the PO_2 in extremities after compression and lifting the blood flow combined with routine blood pressure measurement, described in Paragraph 3.4.4. These data enable us to define a relative parameter for the quality of a certain vessel (or vascular network) and its alteration due to stressful therapeutic influences. In connection with this we should refer to the pilot study into the reduction of the biological age by means of 15 years of O_2 MT (see Paragraph 1.1.6).

5.3.10 Stroma, rheumatism, skin

The new formation of *stroma*, an energy-requiring process, occurs in the living organism wherever larger cell aggregates have decayed. Since this can occur anywhere in the organism and since the local tasks and potential of this reaction are consequently very varied (healing of all types of wounds, broken bones, tissue necroses etc.), the great variety of processes which transform biological material into stroma is easy to understand. One pathological process of this type, the unspecific mesenchyme reaction in the walls of the arterial vessels, triggered by sclerogenous noxae, has already been the subject of several parts of this book.

We will briefly describe one example from the treatment of cancer, as it illustrates the effect of this reaction from a completely different viewpoint: after a first strong therapeutic attack (cancerostatics, ionizing radiation) on a carcinoma, the cancer cells near the capillaries, in particular, which are well supplied and therefore proliferate rapidly, are killed. Just 3 days later histology shows that a *strong mesenchyme reaction (infiltration) has occurred at the site of the destroyed cancer cells near the capillaries*. This mesenchyme prevents the further diffusion of substrates, and the cancer cells distant from the capillaries and not destroyed by the primary therapeutic attack become very resistant to further therapeutic attacks. It was on this process that we based our mesenchyme theory [428] of the formation of resistance in cancer therapy protocols with fractionation.

A chance clinical observation taught us that *wound healing can be promoted and very greatly accelerated* by the interaction of long-term variants of the O_2MT . In one patient trophic disorders after long illness had led to severe decubital ulcers which would not heal. During the course of a 20 h treatment cycle with O_2MT and artificial raising of the blood glucose concentration to four times the normal level, the pressure points closed after approximately 6 days.

This indicates the feasibility of promoting and accelerating wound healing, if necessary also in combination with the stimulation of the body's own defense system.

Good results in the combat of *polyarthritis* using the 36 h (18 day) O_2MT immunostimulation, GK 4-IV variant (with thymus dragees) have been repeatedly reported. We would also refer to the administration of *interferon* [392] as an additional step.

Via the capillary fluid spaces of the *joints* and

bones the O_2MT should also be able to aid in these areas in some disease processes. We are thinking here particularly of the alleviation of inflammatory processes [429–432] and harmful metabolic deposits in the complex rheumatic process by means of the raising of the O_2 metabolism, especially the permanent raising of the product $\eta \cdot COP$ (relative characteristic value) and the stabilization of the lysosomes. Indeed, the O_2MT has proven to be so effective in the framework of rheumatism therapy (natural inhibition of inflammation and mesenchyme reaction, no side-effects as in cortisone derivatives), that its introduction into the *combat of rheumatism* is progressing well.

We must also mention the observations of a significant improvement of knee joint arthrosis (Dolina, Karlovy Vary, CSFR) and of the normalization after O_2MT of considerably raised triglyceride or cholesterol levels which had existed for years, and of increased blood sedimentation rate, for which no cause could be found.

Klopsch has reported on the improvement of the O_2 status after *chiropractic treatment*.

In connection with this we would refer particularly to combinations with the new high-frequency method (CMT Selectotherm procedure), discussed in Paragraph 1.2.2, which enables a high dose of heat energy to be transmitted even to stroma lying deep below the body surface.

Many years before the discovery of the O_2MT procedure and its effect of permanently raising the O_2 uptake, the procedure was performed in 1971 with roughly the same schedule as today on a then 64-year-old male, and was continued until 1980 at intervals of approximately 1 year. The pretherapy PO_{2-art} in 1971 was, on average, 78 mmHg and was only slightly above the expected level for the age of 64. From the beginning of 1977–1980 levels of the PO_{2-art} at rest of between 95 and 105 mmHg were normally found. At the age of 64, the skin on the face (eyes) was already showing clear signs of age. It was striking that these signs of age hardly increased up to the age of 78 years, i.e. until the end of 1986 (latest observations). If this first individual finding is later statistically proven, this would mean that the *ageing of the skin* can be delayed by permanently raising the arterial, and reducing the venous PO_2 at rest.

We have recorded 7 cases in our Institute in which female O_2MT patients spontaneously reported better skin tension (turgor), reduced



Fig. 266 Amelioration of possibly precancerous skin lesions in the back of a 73-yr-old male patient within 10 months through daily intake of a thymus dragee¹ and the securing of a permanently good O₂ status ($\eta \approx 40\%$; resting $\dot{Q}O_2$ 0.34 l/min⁻¹) by 15 min O₂MT quick procedures. Daily brushing of the affected skin areas for 20 s. Left: 1.1.1984; right: 1.11.1984

¹ Thym-Uvocal® (Dr K. Mulli KG, D-7844 Neuenburg, FRG)

skin impurities (comedones) and improvement of acne.

Figure 266 shows an example of the effect of

an O₂MT long-term variant, with the daily administration of one thymus dragee over 10 months, on the skin of a 73-year-old patient.

5.3.11 Defense. Multistep stimulation of the cellular defense

In the same way as the condition of the vascular system, the condition of the defense system is also of decisive influence on the individual's health status. It is known that the organism has a series of mechanism to defend itself from harmful living or dead matter:

1. *Unspecific mechanisms* by co-operation of certain types of cells, the *unspecific cellular defense* and, mediated by soluble factors, the *unspecific humoral defense*.
2. *Specific mechanisms* through highly specific chemical reactions, the immune reactions. Here the organism forms a quite specific defense substance, the *antibody*, against a defined noxa, the *antigen*. Its damaging properties are neutralized by binding the antigen to the specific antibody and its ensuing breakdown (antigen-antibody reaction). The immune globulins represent the fraction of antibodies within the blood serum proteins (specific humoral defense). T-lymphocytes together with other defense cells mediate the specific cellular defense.

All these defense mechanisms need energy, and consequently oxygen.

The main weapons of the *unspecific cellular defense*, the great contribution of which to the defense process has recently been clearly seen, are the polymorphnuclear cells, and the carriers of the specific cellular defense, the T-lymphocytes. One way of increasing the host's defense is to raise the number of these cells in the blood. One way of doing this is discussed further below (see Paragraph 5.3.13.4). Another way is to increase the impact of the defense cells in general or their functional elements on the respective target, in particular by means of energy-raising O₂MT procedures.

With our subject matter it is obvious that we should ask about the *changes in the host's defense system with advancing age*. The critical decline in the provision of effector substances with advancing age should be mentioned here. An example is the drop in thymus products in the plasma as a result of the advancing involution of this gland (cf. Fig. 239). We have found no indication of significant changes in the number of defense cells with age. By contrast, it is reported in [433] that certain *autoantibodies* continuously increase from the age of about 70. Increasingly autoaggressive im-

munological reactions occur from this age, perhaps conditioned by the influence of the increasing O_2 deficiency. This means that the defense system begins to destroy the organism's own cells, i.e. to work where it should not. It is undisputed that a decline in the strength of the host's defense mechanism coincides in old age with the deterioration of the energetic situation. This decline can be at least alleviated by the application of suitable variants of the O_2MT [434].

A very great activation of the host's cellular defense system can be attained if the O_2 uptake of the body tissue is increased by means of intensive variants of the O_2MT . They achieve a temporary increase in the O_2 uptake to over 65% of the mean level for that age, under resting conditions. Three synergistic actions are stimulated by this increase:

1. The energy-consuming locomotion of the defense cells is facilitated.

2. The chemotactic attraction of the defense cells to the target area is promoted.
3. Most of all, the formation of peroxides in the phagocytes is strongly supported (peroxides as the main weapon in phagocytosis; Fischer and Staudinger, 1980).

When concrete ways now take shape to mobilize the host's defense system to some powers of ten more than natural high fever, this means that there are great perspectives for the prevention of numerous diseases and for the treatment of rheumatism. Positive reports in [434a] of a prolongation of life and increased quality of life in AIDS patients encourage the setting up of studies into the combat of this disease by the application of the O_2MT immunostimulation procedure (Zöller, Berlin-West). Extraordinary perspectives resulted for the application of the O_2MT immunostimulation in the prophylaxis and therapy of cancer. This is another broad and exciting working field.

5.3.12 Adaption of the anticancer strategy to advance in tumor immunology

As early as the 1930s there were findings indicating that the growth of malignant tumors might probably be influenced by the body's defense system [435]. The question, asked even then by Domagk, of the significance of such observations from experiments on laboratory animals for the therapy of tumors in humans [436], i.e. of the possibility of an effective immunological treatment of cancer, was still the subject of debate four or five decades later [437, 438]. One of the reasons for this, apart from the well-known difficulties in defining and recording the immunological situation (status) of a patient, is that it is not easy to objectify and assure the efficacy of an adjuvant immunological measure, and it is hardly possible to achieve remissions in diagnosed, i.e. advanced tumors by means of immunological treatment alone. The situation is quite different if the immunological measure hits a conglomerate of cancer cells which is just in the yet undetectable, very early stage of autonomous organization. The author's concepts of prevention of metastases and relapse [38] and of a general cancer prophylaxis [19] are examples of this. In these cases there is the well-founded prospect of destroying the malignant neoplasm *in statu nascendi* and preventing the manifestation of the neoplasm, including metastases and recurrences.

The immunotherapy, as an adjuvant procedure at least, is in the process of gaining great clinical

significance. The number of interesting results with "immunomodulators" is constantly rising. Besides BCG and 2-cyanoethyl urea (CEU) [341, 439], the thymus extracts in particular, highly efficacious even when administered orally [342, 347, 440], have gained considerable significance. Combinations with the preparation PIND-AVI [343, 441] should also be mentioned here, as should also Neythymun [325, 344, 442] and more recent American immunomodulators such as Bestatin [345], and endotoxins and synthetic lysolecithins [443, 444].

It is strange that, in the great advance of tumor immunology, the very great influence of the O_2 status in the organism on the strength of the host's unspecific cancer defense has been disregarded by researchers worldwide. This neglect is surprising because it should be clear that all immunological mechanisms (e.g. attraction and locomotion of the defense cells to the focus, phagocytosis, formation of peroxides as weapons) are of an energy, i.e. oxygen-requiring character. The neglect of the O_2 status and its dynamics in tumor immunology has had two serious consequences:

1. the considerable deterioration in O_2 status and hence in defense due to the stress [20] of chemotherapy and radiation therapy [18] remained almost unknown, as did also the favorable conditions for metastasis arising as a result of this [36] and

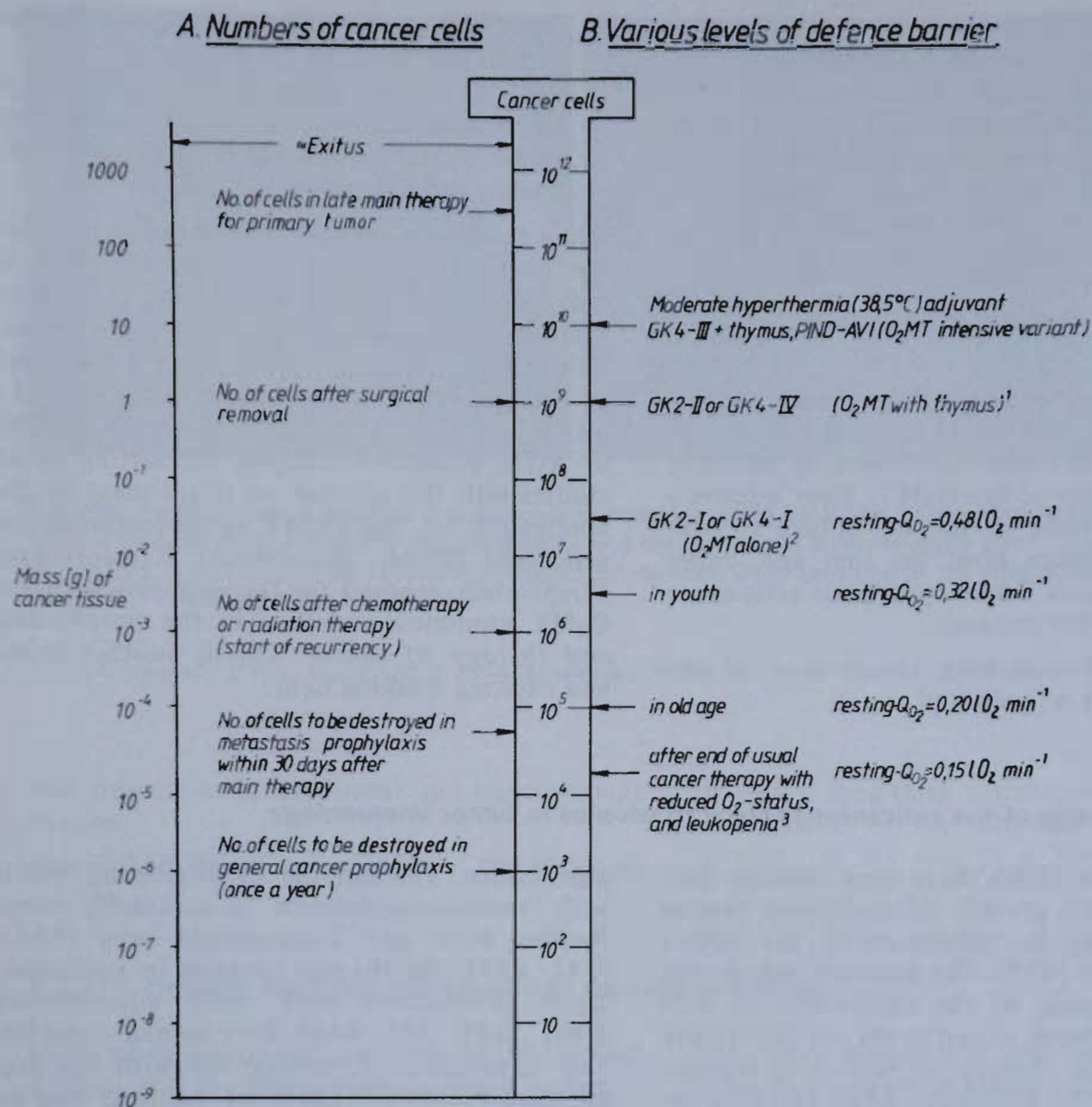


Fig. 267 Number of surviving cancer cells (A) after classical therapy measures (K. Zänker, 1985), and cells to be destroyed in metastasis prophylaxis or general cancer prophylaxis, compared with the approximate levels of the defense barrier (B) in the various variants of O₂M immunostimulation, and in the various levels of the resting O₂ status. Guiding levels

¹ Extrapolated from the disappearance of cancer foci having a mass of 1 g; ² Extrapolated from the disappearance of a basiloma having a mass of $2 \cdot 10^{-2}$ g; ³ Extrapolated from the number of cells disseminated by the primary event of metastasizing based on the assumption of 2 doublings and a mean rate of metastasis of 50%

2. developing O₂MT procedures for the lasting significant improvement of the O₂ status and hence the defense [7, 18, 36, 338] remained unused.

By contrast to the situation portrayed, the method of increasing the host's cancer defense by means of raising the O₂ status combined with the application of immunomodulators has been followed since 1970 in the framework of Dresden oxygen and cancer multistep therapy research [2, 143, 454]. The result was the present variants of the "oxygen multistep

immunostimulation" [18, 19, 38], the steps of which are part of clinical trials [19] based on the 1974 CMT concept [143].

In Fig. 267, derived from these thoughts and the experimental findings quoted, the number of cancer cells surviving a conventional tumor therapy and the number of cancer cells to be destroyed by a metastasis or general cancer prophylaxis program are compared to the various levels of the defense threshold which varies within six powers of ten, depending on the conditions described in the figure. The guid-

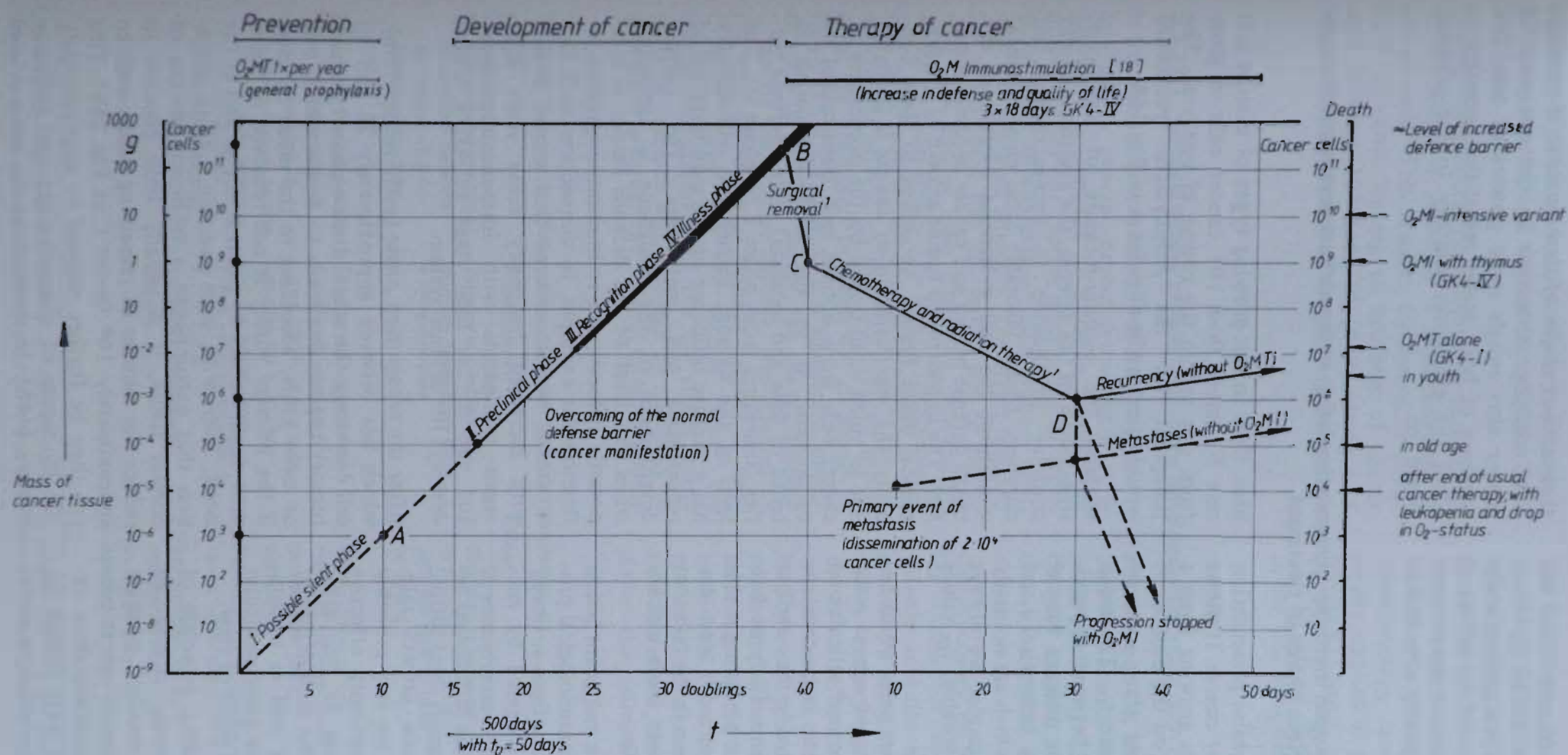


Fig. 268 Cellular development of cancer and combatting the primary tumor by the present usual types of therapy, with supplementation (support) by O_2MT immunostimulation (O_2MI), 3x variant GK 4-IV ($3 \times 18 = 54 \text{ days}$). General cancer prophylaxis at a cell number $\leq 10^3$ (A). Metastasis therapy at a cell number 10^5 to 10^7 (D). The aims and effects of the adjuvant O_2MI are the reduction in the metastasis rate, increase in the cure rate, and increase of the circulation reserves and quality of life, which have been reduced by chemotherapy or radiation therapy. Basic principle: combatting cancer in stages with low number of cells!

ing values of the right-hand ordinate reflect the *augmented defense potency*, when the O_2 status and the variants of the O_2 MT are appropriately considered. From the numbers of the left-hand scale the guiding principle can be drawn that *tumors should be immunologically attacked in*

their earliest stages of development, if possible. The resulting advantage in the conquest of cancer also equals some powers of ten. The numbers of both scales reveal the necessity to adapt the anticancer strategy to the progress aimed for.

5.3.13 Application of the oxygen multistep immunostimulation in the various development stages of tumors and in various phases of treatment

Figure 268 shows a comprehensive presentation of the *cellular development of cancer*. It shows the avalanche of cancer cells growing from a single cancer cell, dependent on the number of cell doublings. The following time scale represents the cell doubling time t_D . The mean value of t_D is known to lie between approximately 50 and 200 days for primary tumors and significantly shorter, e.g. between 10 and 50 days, for the metastases, which are normally better supplied. In later examples we always assume the smallest (least favorable) t_D values of the named areas.

It is assumed today that cancer cells, which become the start of avalanches of cancer cells, arise relatively often from normal cells due to carcinogenic influences. These avalanches are normally caught and eliminated in their earliest stage by the unspecific defense (defense barrier). The regulating principles prevailing in this *possible silent phase* have already been discussed in [376]. They were seen in the fact that the power of defense increases more quickly than the number of cancer cells.

The host's "recognition" of a malignant lesion is not necessarily a specific immunological process in the sense of a classic antigen-antibody reaction, but is frequently triggered by anomalies in the metabolism and/or membranes of the transformed cells [447]. The differences between numerous tumors as regards localization, timepoint of their appearance, growth rate, metastasizing propensity etc. are very probably conditioned by the host's variously effective control mechanisms. As long as this great variety remains unscrutable, the *stimulation of unspecific* (immunological as well as non-immunological) *defense processes* gains particular significance from the practical point of view.

In accordance with the *guiding principle of implementing the immunological combat of cancer in stages with the smallest possible number of cancer cells*, the general cancer prophylaxis with O_2 MT immunostimulation repeated approximately once a year should be given top priority among the combative meas-

ures. Even in fast-growing types of tumors it is rare for more than 10^3 cancer cells to grow from one cell in the course of one year. The timepoint for the prophylactic procedure would therefore lie at point A in Fig. 268.

Without the counter-measure of significant stimulation of the defense, the avalanche would continue to develop to ever-increasing cell numbers. Under favorable local environmental conditions the cell avalanche overcomes the host's defense barrier and *cancer becomes manifest*. The uncontrolled tumor growth of the pre-clinical phase begins. According to these concepts, the *manifestation of cancer* is probably not so much conditioned by the occurrence of cancer cells from normal cells transformed by carcinogens, as by the level (fluctuating in terms of time and location) of the defense barrier (transition from phase I to phase II). The level of the defense barrier also undoubtedly has a decisive influence on the manifestation of recurrences and metastases. The further development of the avalanche is facilitated when the level of the defense barrier is temporarily reduced, due to immunosuppressive influences for example. In connection with this it should be remembered that cancer occurs with increased frequency some years after organ transplants with immunosuppression, and also in the final stage of AIDS, which destroys the defense system.

After the *recognition phase* (early recognition), which lies between approximately 23 and 30 cell doublings, the actual disease phase (primary tumor) begins; this leads to death within one or more years, according to the mean t_D rate; if the primary tumor is not removed in time, then death occurs by point B in Fig. 268 at the latest. Even with wide excision, i.e. an operation that encompasses a sufficient margin of normal tissue, it is usually only possible to reduce the number of remaining cancer cells to approximately 10^9 (point C in Fig. 268). This can then be further reduced to approximately 10^6 by means of chemotherapy and radiation therapy [448]. In many cases the natural level

of the host's defense is not sufficient to destroy 10^6 cancer cells, and tumors recur (point D in Fig. 268).

During the classical therapeutic measures mentioned there is generally a dissemination of cancer cells. This triggers metastasis in about 50% of cases, leading to numbers of cancer cells between 10^5 and 10^6 [449] within 4–8 weeks after treatment of the primary tumor.

The O_2MT immunostimulation, applied at point A of Fig. 268, would serve to realize a general cancer prophylaxis; applied shortly before point B, it can reduce the risks in surgical tumor removal; applied between points C and D, it can increase the quality of life and effectiveness of chemotherapy and radiation therapy, and, finally, applied at point D, it can provide a prophylaxis against metastases and recurrences. The details of these applications are discussed in the following paragraphs.

5.3.13.1 General cancer prophylaxis in the developmental stage with only 1000 cancer cells

It has already been pointed out that, in order to establish a *general cancer prophylaxis*, it is necessary to simplify as much as possible the procedure for the certain destruction of aggregates with approximately 1000 cancer cells, which is repeated annually. The effort required for a procedure like this should not be greater than the annual mass miniature radiography, which is usual today. The task of simplification also applies to O_2MT immunostimulation. The synergistic effects of this two-pronged procedure are portrayed in Table 43. As shown in Paragraph 4.2.4, Fig. 227, a significant simplification of the first factor, the chemical stimulation of the cellular defense, was attained by the administration of thymus dragees or Neythymun drops. For the second factor, the lasting improvement of the O_2 status, many years of research will probably be necessary to determine whether the 15 min O_2MT immuno-

stimulation, GK 2-II variant, or even just the improvement of the O_2 status by means of drugs (cf. Fig. 235) in combination with thymus dragees or Neythymun drops are of clearly detectable efficacy in the prevention of cancer.

Our discovery of the great significance of the O_2 status for the host's unspecific cancer defense is quite new and therefore not yet generally recognized. Figure 269 therefore shows an experimental finding that clearly shows the *influence of changes in the O_2 status on the strength of the host's cancer defense*. A basiloma of approximately 25 mm^3 was observed in a patient having an initially good O_2 status ($\eta = 52\%$). Then he had influenza, which caused his O_2 status to deteriorate severely to $\eta = 14\%$. As a result of the concomitant reduction in defense, the basiloma grew to 140 mm^3 . After the influenza the good O_2 status re-

Table 43 Synergetic effects of O_2 multistep immunostimulation

Step	Phenomenon	Effect	Literature
1. Chemical stimulation of cellular defense by means of BA1 effect or thymus extract	Temporary increase in number of leucocytes + lymphocytes	1. Significant increase in number of defense cells for several days to weeks	von Ardenne-Reitnauer (1975 until 1980)
2. Energetic activation of cellular defense by increasing O_2 transportation to the whole body tissue with variants of O_2 multistep therapy	Temporary increase of O_2 transportation to up to 250% of the average rate for a 70-year-old, for some days. Triple synergistic effect. 2.1/2.2/2.3 Increased phagocyte activity	2.1 Stimulation of cell motility through improved energetic situation ¹ 2.2 Stimulation of chemotactic attraction 2.3 Stimulation of formation of peroxides in the phagocytic cells ¹	von Ardenne (1979 until 1980) Richter (1980) Fischer-Staudinger (1980) (role of peroxides as principal weapon at phagocytosis)

¹ Energy/ O_2 consuming processes. An idea of the strong influence of the O_2 status alone on the potency of the cellular defence, can be gained from the in vivo observation of a basiloma in Fig. 269

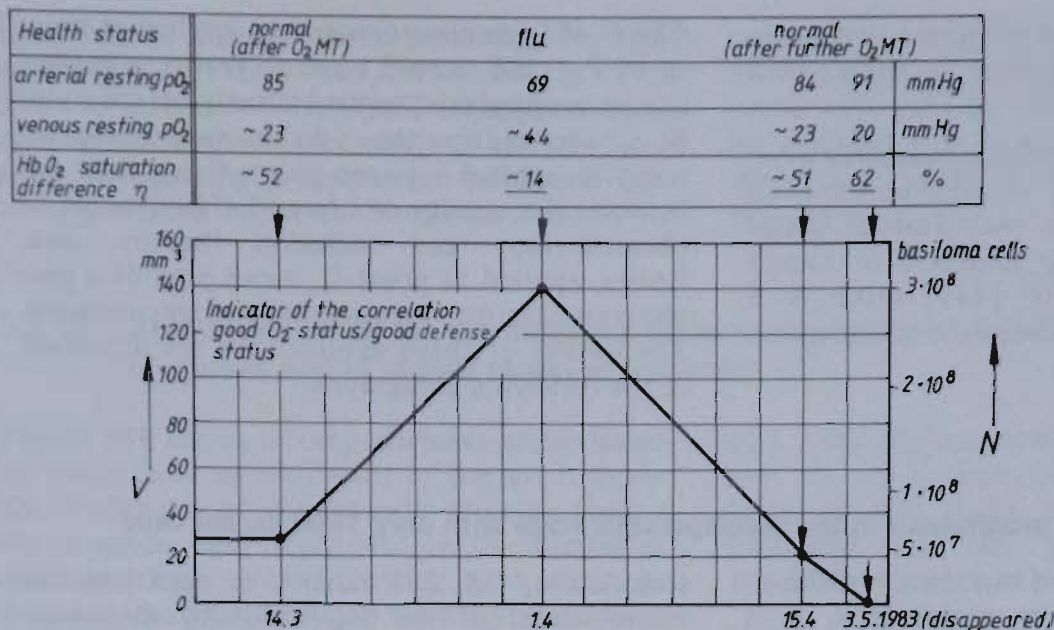


Fig. 269 Example of the dependence of the steady state between the new formation of cells and cell destruction by the host's cellular defense system, on the O₂ status of the organism (basically, the η level is decisive here), in a basiloma. Destruction of at least $5 \cdot 10^7$ basiloma cells by O₂MT alone (Variant GK 2-I), male, 76 yrs

turned, and the size of the basiloma dropped to approximately its initial dimension. A very good O₂ status ($\eta = 62\%$) was then attained long term by means of the O₂MT procedure, and the skin basiloma disappeared. In this paradigm the *improvement of the O₂ status was enough to increase the host's defense so as to destroy $5 \cdot 10^7$ cancer cells*. According to Figs 267 and 269, the raising of the O₂ status by means of the 15 min O₂MT quick procedure GK 2-I (implemented once or twice) should be sufficient to make possible a general cancer prophylaxis with considerable reserve power when repeated annually – certainly when combined

with the administration of thymus dragees or Neythymun drops over several weeks. The author is at present trying to arrange a large-scale study with 6000–10,000 volunteers and a duration of approximately 5 years for this question.

The intervals between repetitions for general cancer prophylaxis are determined by the size of the avalanche of cancer cells held to be just tolerable, and by the shortest cell doubling time to be considered. Figure 270 shows a presentation of this.

The *schedule of a procedure for general cancer*

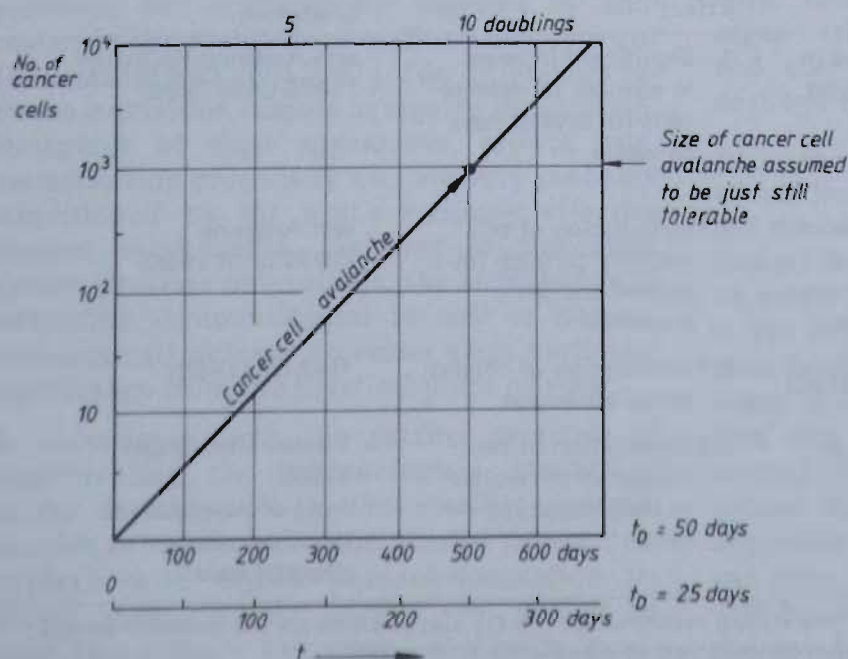


Fig. 270 A cancer prophylaxis procedure which destroys foci of 10^3 cancer cells should be repeated once a year, when the cell-doubling time is $t_D = 50$ days¹

¹ The average cell doubling time is in most tumors between $t_D = 60$ and $t_D = 200$ days

prophylaxis with great reserve for the destruction of cancer cells roughly corresponds to the schedule of the 15 min O_2 MT immunostimulation GK 2-II, which has already been shown in Fig. 228 (although without the PIND-AVI preparation). An extremely simple prophylaxis

with smaller, perhaps not quite sufficient, reserves for the destruction of cancer cells could exist with the oral administration of one ginseng capsule and one thymus dragee daily over a period of 45 days.

5.3.13.2 Reduction of the risks in surgical tumor removal

A significant deterioration in the O_2 status occurs in the surgical removal of the primary tumor, mainly due to narcosis [20]. This drop can lead to the triggering of severe crises (cardiac arrest, cardiac arrhythmia, myocardial infarction, circulatory insufficiency etc.) in persons with a poor O_2 status, elderly patients for example. For elderly patients subjected to severe distress it is therefore advisable to raise the O_2 status and hence the circulatory reserves

before the operation by means of *preceding* O_2 MT [108]. The GK 2-I variant described in Paragraph 4.2 should be used for this for patients who are still capable of exertion, and the GK 4-I variant for those who are not. After extended operations it is also advisable to use the GK 4-IV variant in the rehabilitation phase in order to accelerate wound healing and general recovery, and to reduce the number of surviving cancer cells.

5.3.13.3 Chemotherapy and radiation therapy: increase in efficacy and quality of life

If the circulatory reserves drop critically about 20 days after the start of cancer treatment cycle using drugs or irradiation, it is well known that there is such a significant reduction in the quality of life that the patients often refuse the continuation of these measures that are neces-

sary for them. The extent of the circulatory complaints is determined by the energetic status of the organism (provision of energy-rich phosphates), and under normal living conditions this status depends almost exclusively on the O_2 status of the body, at rest. From meas-

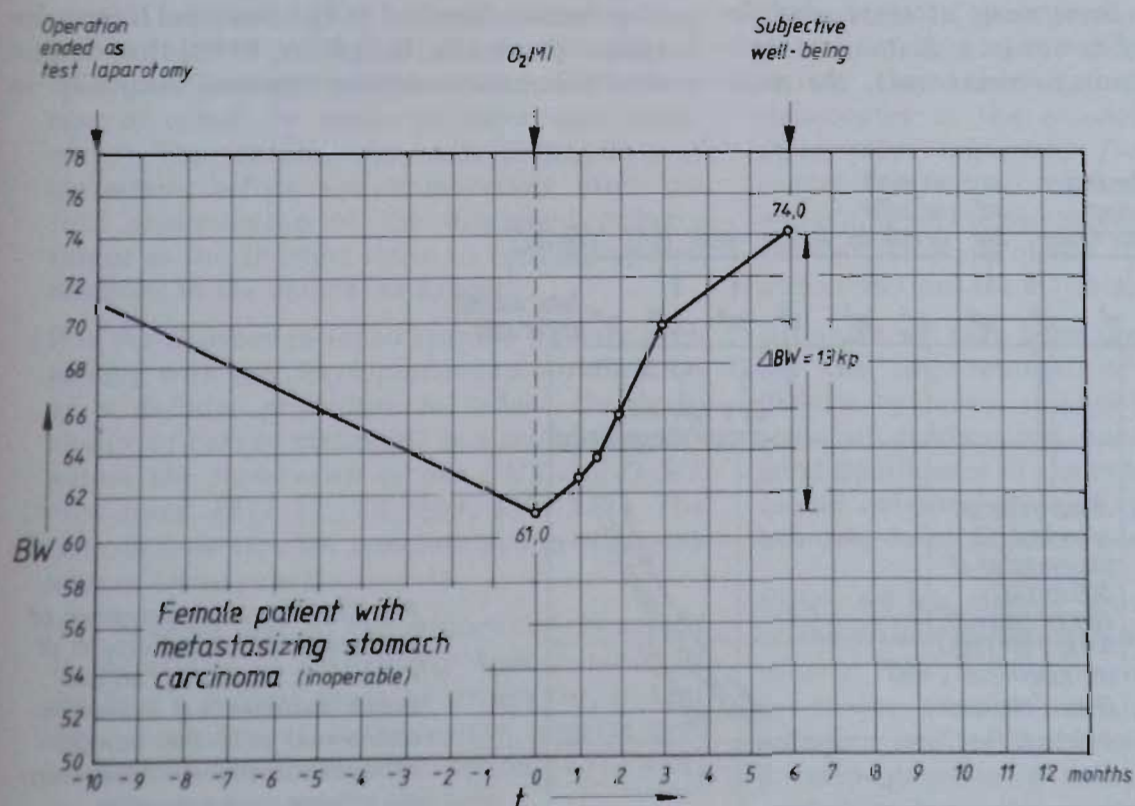


Fig. 271 Body weight (BW) changes and further course of the disease in an inoperable 73-yr-old cancer patient before and after O_2 multistep immunostimulation (O_2MI)

urements of the O_2 status we found that, with a certain delay, a severe deterioration of the O_2 status accompanies irradiation and chemotherapy as is generally the case when other toxins invade the circulation. The cause of the drop in quality of life in such phases (pre-collapse condition, loss of appetite, weakness etc.) must be seen in this phenomenon. However, we also found that the poor O_2 status can be raised back to good levels by means of the procedures of the O_2 MT already discussed, and that consequently a *great increase in the quality of life* is observed. Figure 271 shows an example of this: an elderly female patient with an inoperable stomach carcinoma, metastases, severe pain, dizziness and nausea, already in cancerous cachexia. After the procedure her life became worth living again. The pain and complaints disappeared, her appetite returned and her weight

rose by 13 kg. In this example from our Institute, as in other cases mentioned, the defense barrier was probably raised by more than 10^4 to approximately 10^9 cancer cells.

For both irradiation and chemotherapy of cancer, when performed without the adjuvant O_2 MT immunostimulation, dose splitting (fractionation) is necessary in order to ensure that the invasion of toxins does not lead to circulatory disorders and that the leucopenia does not fall below the limit of 2000 cells/mm³. If, however, the O_2 MT procedure GK 4-IV is implemented at the same time as irradiation and chemotherapy, this results not only in the advantages already mentioned (gain in quality of life etc.), but also in the ability to apply higher doses (increased effectiveness) and fewer fractions (time saving). The advantage has hardly been acknowledged and utilized as yet.

5.3.13.4 Prophylaxis of metastasis and formation of recurrences

It is known that *over 80% of all cancer deaths are caused by metastases* and only about 10% by the primary tumor [449]. Furthermore, the literature has shown that the probability of metastasis increases very quickly the larger the primary tumor (advanced stage) at the time of the first treatment. An example of mammary carcinoma, in accordance with [451], is shown in Fig. 272. *For mean tumor dimensions at the time of the first therapeutic attempt, and for common types of tumor (e.g. mammary carcinoma, lung carcinoma, melanoma), the prob-*

ability of tumor dissemination lies at 50–60% or even higher. In the individual case the discovery of metastases normally means a considerable reduction in life expectancy. The facts indicate that the *development and testing procedures to combat cancer metastasis are the main responsibilities of current cancer research.* That this must be taken very seriously and challenges us to fast action is based on a statement of a former director of the National Cancer Institute (Bethesda, MD, USA, 1980) that despite the billions of dollars invested annually in

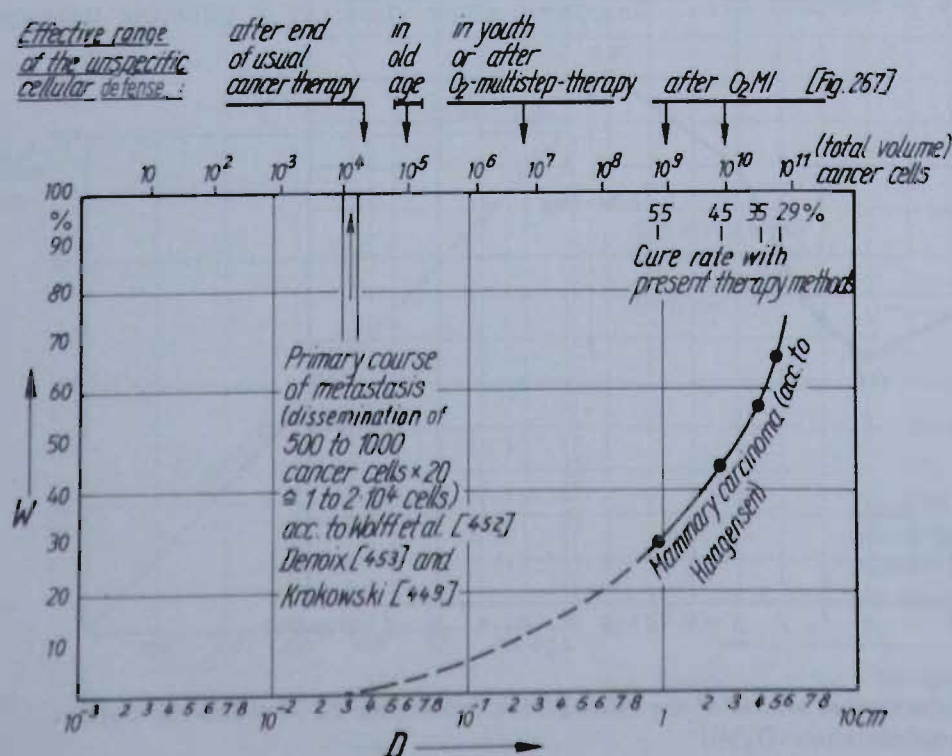


Fig. 272 Primary mechanism of metastasis and probability W of metastasis, dependent on the tumor diameter (e.g. mammary carcinoma) or on the number of residual malignant cells escaping surgical, radiological or chemotherapeutic treatment. With application of details given by E. Krokowski [449]

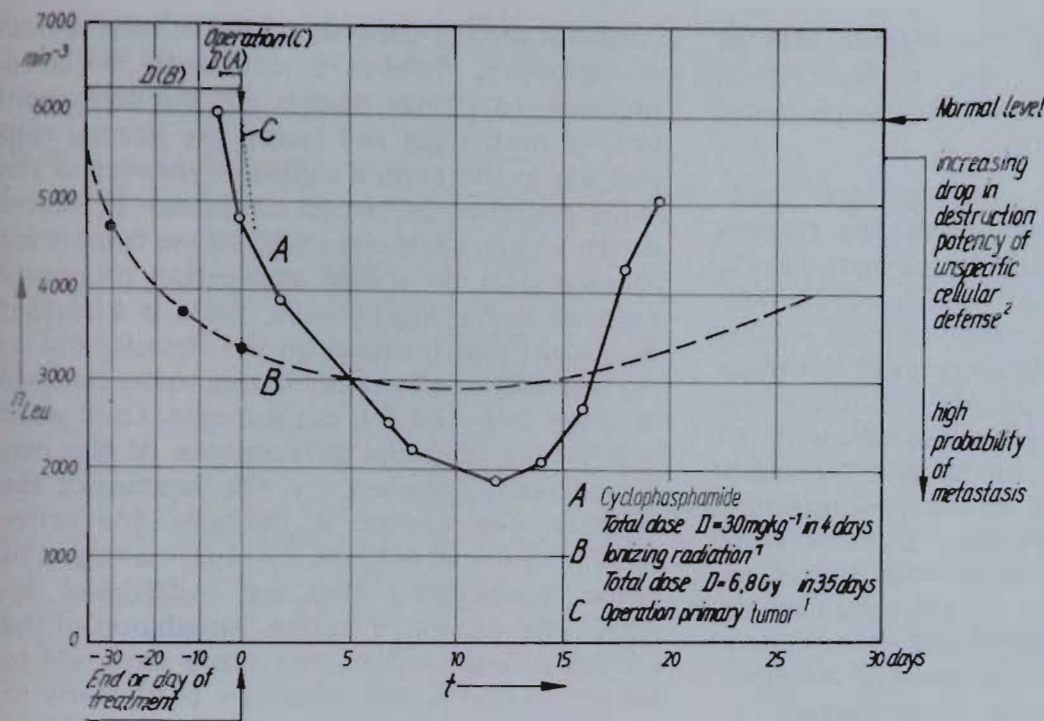


Fig. 273 Measurement examples of the drop in the number of leucocytes n_{Leu} (leucopenia) after a single effect of cytostatica (A), ionizing radiation (B) and surgical treatment (C)

¹ Volume of primary tumor $\approx 800 \text{ cm}^3$; ² Reduced pH level in the cancer tissue increases chemotactic attraction

cancer research worldwide, there has been no change in the relative number of cancer deaths in the last few decades. In his pioneering criticism of present-day procedures in the combat of cancer [449], Krokowski states and proves that "in the last 20–25 years it has not been possible significantly to improve the cure rate of cancer by means of therapeutic measures." This author, too, sees prophylaxis of metastasis before and immediately after the first manipulation of the diagnosed primary tumor as the shortest route to opening up new horizons to the combat of cancer.

For the above-mentioned reasons we have been dealing with the development and optimization of a definite procedure to reduce the probability of cancer metastasis in a series of papers within the framework of our CMT and O_2 MT ever since 1971 [2, 38, 309, 310, 311]. The time is now ripe for concrete action along the lines of these papers.

It is obvious that, at the moment of the spread of metastases, a particularly high potency of the host's defense must be striven for, so that the probability of dissemination remains low. In present-day therapeutic action [457, 458] the opposite is normally the case.

Immunological research since 1970 has shown increasingly clearly that the unspecific cellular

defense makes the main contribution to the combat of cancer by the host's defense system. The number of defense cells (leucocytes, T-lymphocytes) in the blood per unit of volume is therefore of great importance for the functioning of the cancer defense. As Figure 273 shows, the concentration of defense cells (leucocytes in the example) drops with the three most important forms of present-day cancer treatment: leucopenia. This means a weakening in the cancer defense in the phase of the dissemination of the cancer cells, i.e. favorable conditions for metastasis.

Although we have been suggesting and examining the improvement of the host's cancer defense by means of O_2 MT procedures, in the series of publications quoted since 1971, the great significance of the individual O_2 status for cancer defense, which is visible from Fig. 267, has only been discovered in the last few years.

Figure 60 has already shown typical examples of the critical deterioration in the characteristic value η (O_2 status) immediately after the end of cancer therapy with cytostatics, ionizing radiation and surgical tumor removal. The discovered drop in η reveals a further major contribution to the weakening of the cancer defense in the phase of cancer cell dissemination. Interacting with the simultaneous drop

in the concentration of the defense cells in the blood, an extremely critical favoring of metastasis can be seen with the conventional cancer treatment methods.

The pathophysiological findings and facts (measurements) discussed reveal the reasons why at present the probability of metastasis is still on average over 50–60% of cancer therapy cases, and why about one million cancer victims must still die prematurely every year. Yet these findings and facts necessarily point to the concrete methodological way significantly to reduce the probability of metastasis: it consists in the temporary raising of the concentration of the defense cells in the blood by stimulating their generation and simultaneous lasting increase in the O_2 uptake of the organism by means of variants of the O_2 MT immediately after the end of the first treatment of the primary tumor (with possible dissemination of cancer cells due to diagnostic or therapeutic manipulation). The term "oxygen multistep immunostimulation" was introduced 1981 for this combined procedure, which has already been dealt with in Paragraphs 4.2.2, 4.2.4 and 4.2.8.

Table 43 gives a survey of the interrelationship of the two basic steps and their synergistic effects in O_2 MI. The O_2 uptake in the body forms the limiting factor for the provision of (chemical) energy. It is not therefore surprising that a lasting improvement in the O_2 status significantly intensifies the various energy-requiring processes (3rd column in Table 43) of the cellular cancer defense.

The strong effect of the immunostimulation might be partially founded in the following

correlations: the capacity of the cellular system of unspecific defense is constantly required, probably to a large degree, for the permanent task of destroying and lysing the normal cells that die in the natural cellular dynamics of the living organism (scavenger function). In cancer patients at an advanced stage, whose tumors are characterized by a high proportion of poorly supplied and decaying cells, there is a further significant passive strain on the capacity due to the necessity of also contributing to the removal of these cells and cell constituents. Only what is left over after the performance of the permanent task discussed, i.e. the remains of the capacity, the excess, is available for active cellular immune defense, i.e. for the types of cancer prophylaxis discussed. Additional defense cells, generated by the stimulation of the cellular defense system over many days, add to the excess and hence contribute particularly to the (partial) recovery of the defense capacity.

There has recently been an advance in the stimulation of the neoformation of defense cells by means of thymus preparations, as it has been possible to separate the immunosuppressive fraction of the total extract from the immunostimulating components, and to concentrate only the immunostimulating peptide mixture in 2 ml (13 mg) ampoules (ISTP thymus preparation by Dr. Jäger, manufactured by Dr. Kurt Mulli, Neuenburg, FRG). Figure 274 shows measurements of the increase in leucocyte concentration up to 25 days after a single administration of a well tolerable dose, using this preparation on Wistar rats. Even thymus preparations from which the immunosuppressive fraction has not been separated, such as the orally administrable dragees (cf. Fig.

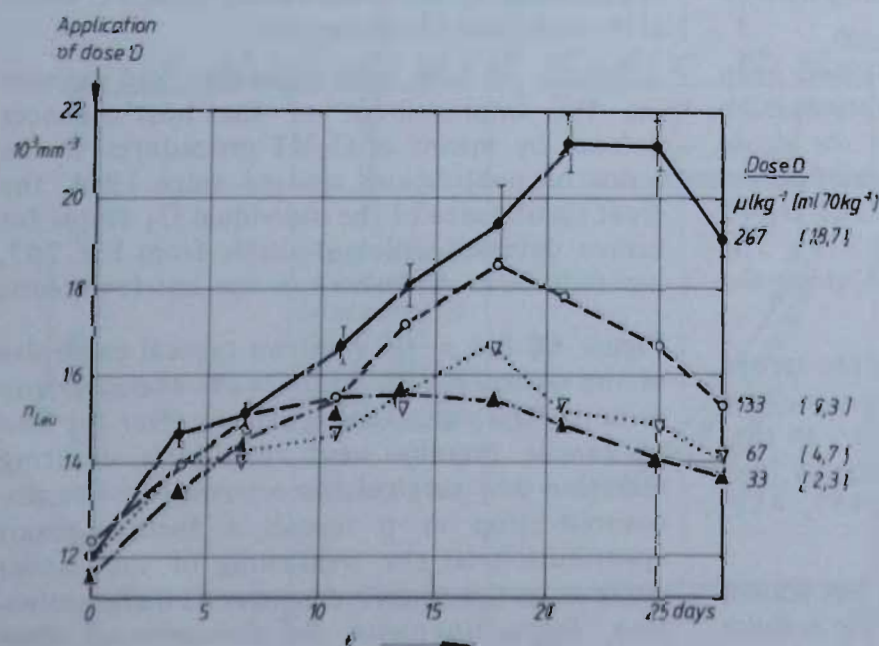


Fig. 274 Increase in the number of leucocytes in the circulating blood after stimulation of the defense system by a single i.v. application of various doses of thymus extract. Conventional male wistar rats (mean body mass 150 g), 5 animals per group. Thymus extract Thym-Uypcal (without immunosuppressive components) from Dr K. Mulli KG, D-7844 Neuenburg, FRG. Expt.: W. Krüger, P. G. Fleitmaner 1983

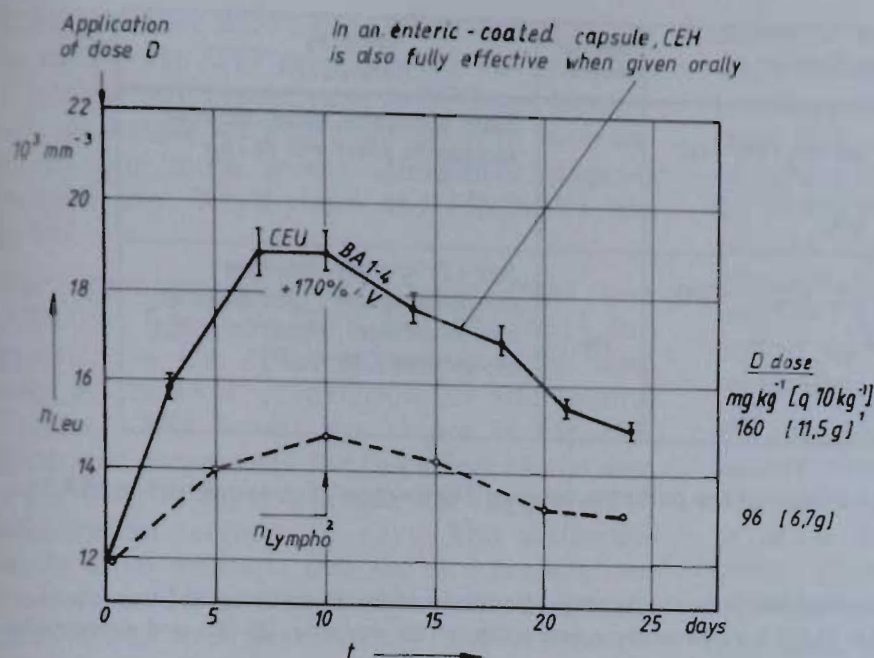


Fig. 275 Increase in the number of leukocytes in the circulating blood of conventional Wistar rats after stimulation of the defense system by a single i.v. dose D of the immunomodulator BA 1-4 (2-cyano-ethyl urea, CEU); expt. P. G. Reitnauer 1978/80

¹ D = 2.7% of LD₅₀ (!)

² The increase in the number of platelets was approximately 29%

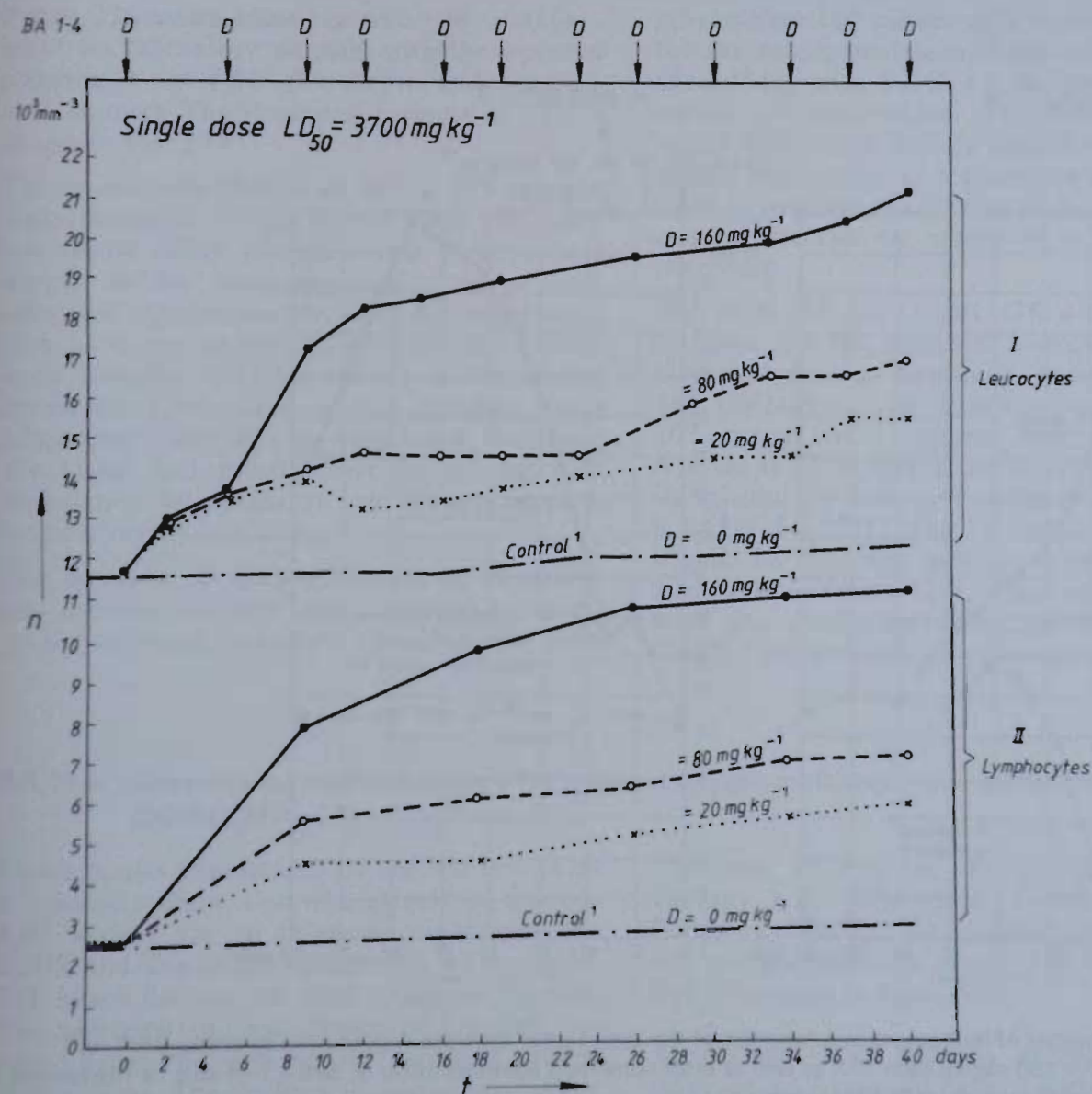


Fig. 276 Leukocyte (I) and lymphocyte (II) counts as a function of the time t in a 40 day stimulation of the host's cellular defense system by application of repeated doses D of BA 1-4 (2-cyano-ethyl urea) as indicated to conventional Wistar rats housed in groups each of $n = 8$

¹ 25% of the animals died in this group probably due to unspecific infections. In the expt. group receiving the 160 mg kg⁻¹ doses no animals died, apparently as a result of a protective effect of the strong and lasting defense stimulation

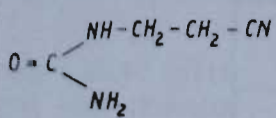
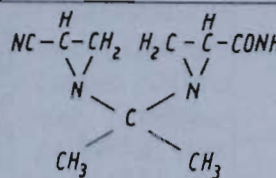
Abbreviation (code)	Name	Structural formula	Molecular weight	Remarks (references)
<u>CEH</u> (BA1-4)	2-cyanoethyl urea (open-chain form of BA1)		113	Easily obtainable, stable, maximum leucopoietic effect with $5 \times 3.4 \text{ g}^{-1}$
<u>CIA</u> (BA1-7)	1-[1-(2-cyano-aziridiny) isopropyl]aziridin-2-carboxylic acid amide		194	Dose: $5 \times 1 \text{ g}$ orally, maximum stimulation at Day 7, also available from Boehringer, Mannheim (FRG), as Azimexon [BM 12531]

Fig. 277 Two derivatives, showing the BA1 effect, of the parent substance 1-carbamoyl-2-cyano-aziridine (BA1), synthesized in our institute [341]

¹ Calculated for 70 kg body weight; i.v. administration in sterile-filtered sodium chloride solution at intervals of 2–3 days; the pure substance (checked by TLC) is sufficiently water soluble (35 mg/ml at 20 °C) and extremely low toxic: LD₅₀ 3700 mg/kg i.v. (rat)

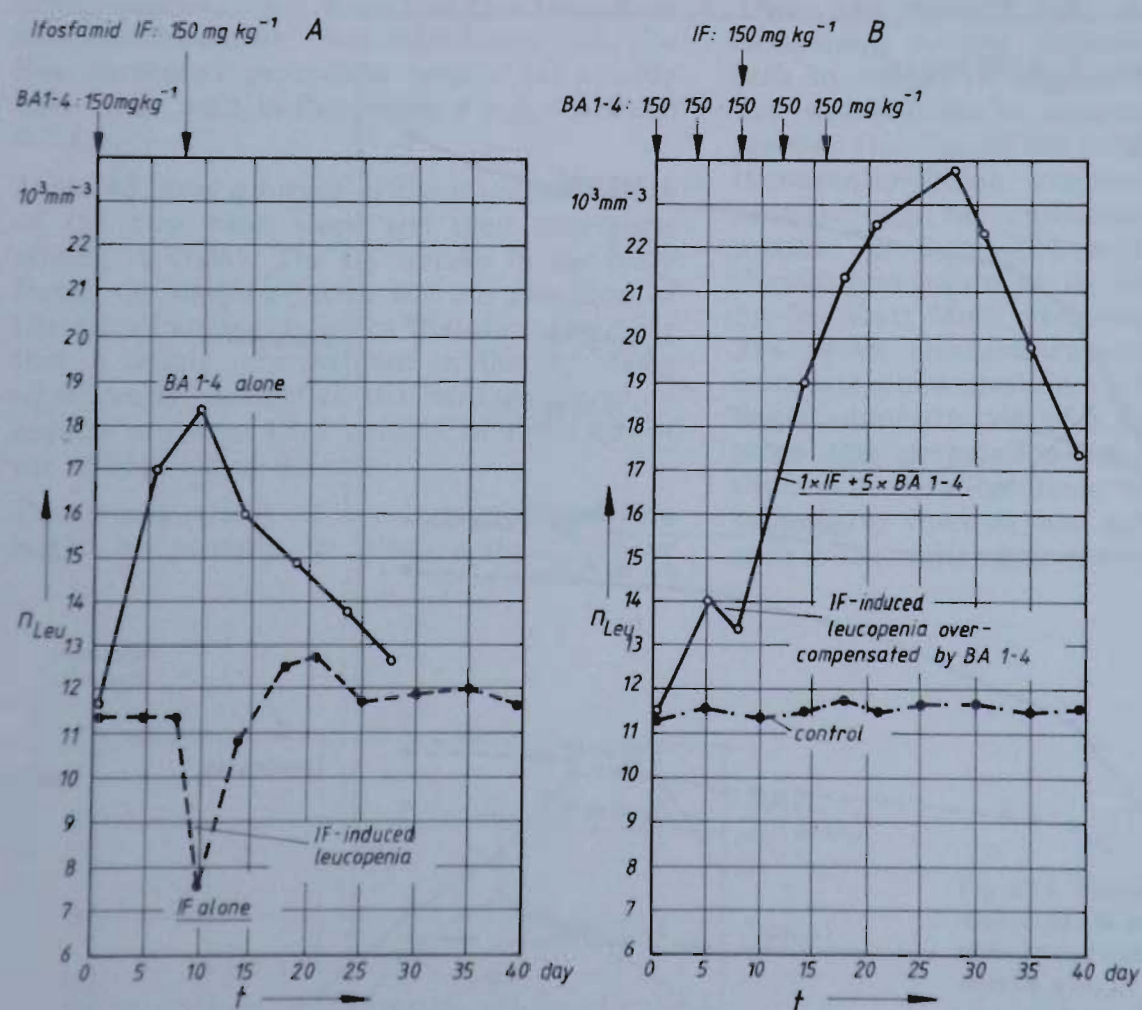


Fig. 278 The number of leukocytes as a function of the time t after separate applications of either BA 1–4 or Ifosfamide. D = 150 mg/kg each (A), as well as after combined administration of 5x BA 1–4 and 1x Ifosfamide at the same doses (B); groups of 8 Wistar rats each

227), still have such a good effect that they can be used if the ISTP preparation is not available. The older stimulants, such as BCG and Levamisole, no longer seem competitive. For measurements on more recent stimulants, such as Neytumorin, Neythymun and PIND-AVI, see [344].

Our immunomodulator 2-cyano ethyl urea (CEU, or BA 1-4) [341, 342, 344, 461], formulated in Fig. 277, was tested in the same way as the ISTP preparation (or also thymus dragees). The results are shown in Fig. 275. With this preparation the full effect can be seen after just 7 days, whereas the thymus ISTP preparation requires 16 days. This difference leads us to conclude that the two preparations operate on different sites of the cellular defense system and to hope that they interact synergistically when combined.

Figure 276 summarizes the result of an experiment on laboratory animals with the *repeated application of CEU* (leucocyte and lymphocyte counts). The structural formula of CEU is shown in Fig. 277.

The animal experiment as in Fig. 278 suggests that stimulants of the named kinds can cause *leucopenia* (after administration of anticancer drugs) to be compensated for or at least alleviated. Unfortunately, the CEU preparation (BA 1-4, i.m. or oral, VEB Sächsisches Serumwerk Dresden, GDR) is not yet on the market (presently synthesized in our Institute on a laboratory scale). For the time being, therefore, the O₂MI will mostly have to get by with stimulation by means of, e.g. thymus preparation or Neythymun alone.

The measures to reduce the rate of metastasis and increase the cure rate discussed by means of the adjuvant procedure of O₂MT have been

clinically confirmed as shown by Fig. 83. A study between 1974 and 1978 on patients with histologically proven cervical carcinoma (mostly stage IIb) showed a drop in the dissemination rate from 30 to 16% and in the death rate from 28 to 8% [461]. This result, which was obtained 5-6 years after treatment, is of great importance because the 1974 concept of O₂MI and CMT [143] has since then been much improved by methodological and technical developments [125, 142].

As mentioned above, the procedure aimed against metastasis should take place, if at all possible, during the cancer treatment with radiation or chemotherapy, also so that the quality of life, which is reduced in this phase, is raised again.

According to Fig. 267, procedural variants that are sufficiently sure to be able to destroy approximately 10⁶ cancer cells should be enough for the supplementation of the cancer therapy usual today with O₂MI, i.e. to combat the formation of recurrences. This sort of variant would differ only slightly from a variant aimed against metastases. It is therefore usually sufficient to perform the combat of both metastasis and recurrences by means of a single O₂MT procedure.

The 36 h (18 day) O₂MI, GK 4-IV variant, is intended for the *practical implementation of the prophylaxis of metastasis*. According to Fig. 267, the high level of its defense barrier (around 10⁹ cancer cells) ensures very considerable reserves as far its destructive effect is concerned. Its schedule is discussed in detail in Paragraph 4.2.4 (cf. Fig. 231). This 18-day variant can and should be repeated several times within the framework of this task, once simultaneously with the irradiation and chemotherapy, and then for the prophylaxis of metastasis.

5.3.13.5 Conventional cancer therapy with adjuvant oxygen multistep immunostimulation (OCR-O₂MI)

Findings and experiences of the last few years increasingly show that the effects of the GK 4-III variant (as an intensive variant) of the O₂MI, and also of the variants GK 4-IV and GK 2-II, *reach far into the field of cancer therapy*. The appraisal of this, drawn in Fig. 267, resulted from the sum of our own and others' observations. The findings in numerous centers of the O₂MT were so impressive that, under the leadership of Dr Wolf (Bad Wildungen, FRG), a doctors' working group for the utilization of the O₂MI was spontaneously formed within the

"Doctors' Society for the Oxygen Multistep Therapy e.V." (President: Dr. R. Holzhüter, Hamburg, FRG). This working group held its 4th symposium with about 200 doctors near Bad Wildungen in June 1986.

Almost all O₂MI findings exceeded expectations: in a 63-year-old patient with a pancreatic carcinoma of approximately 1.5 cm diameter, the carcinoma was no longer detectable about 2 months after the procedure. A significant remission was observed in a patient with an in-

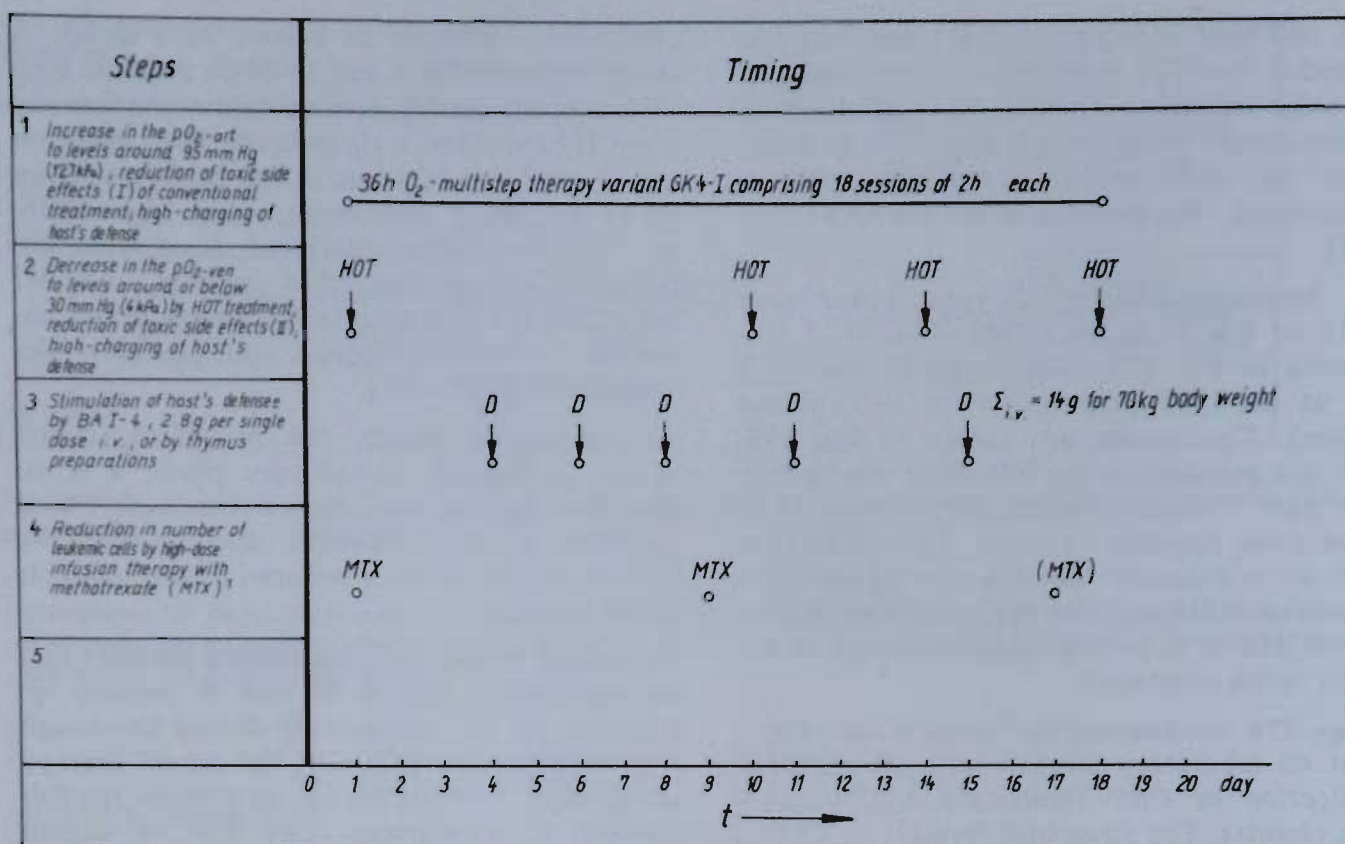


Fig. 279 Example for a program for an anti-leukemic multistep therapy by combining intermittent high-dose chemotherapy with Methotrexate, a several week long strong stimulation of the host's defense system by the immunomodulator BA1-4 (CEU) and the increase in the resting O_2 uptake in the body by more than 60%

operable esophageal carcinoma (Engler, Salzburg, Austria). An exploratory excision in a 58-year-old female patient histologically established a mammary carcinoma and a mastectomy was suggested, but refused by the patient. Four months after treatment, the total remission of the tumor in the right breast was ascertained (Engler). In a 37-year-old patient with liver metastases the total remission of the metastases in the left liver lobe and partial remission in the right lobe were found after 8 months. The patient is going to return to work (Engler). In a female patient with a mammary carcinoma of approximately 1.5 cm diameter, who had refused a mastectomy, a complete disappearance of the tumor was established 2 months after treatment (Wolf). In *cancer patients with advanced metastases* (liver, skeleton), X-rays showed a stop in progression in 5 out of 7 cases over the observation time of many months. In leukemia, treatments with the schedule given in Fig. 279 (high dose interval chemotherapy, increase in circulatory reserves) achieved a significant rise in therapy effectiveness.

Results of this kind, and the basic principle of immunologically combatting cancer in stages with as few cancer cells as possible, led the author to the following *generalizing form of*

therapy, which has already proved successful in not a few cases of advanced, metastasizing cancer stages: classical cancer therapies¹ with adjuvant triple procedure of oxygen multistep immunostimulation (O_2MI): OCR- O_2MI .

In the first stage of therapy every attempt is made, in the current classical form, to minimize the number of surviving cancer cells: surgical removal and radiation therapy of the primary tumor; also chemotherapy, especially when there are already metastases (Fig. 268, target: number of surviving cancer cells $< 10^6$). Then a second adjuvant measure in accordance with Fig. 280, the variant of 36 h (18 day) O_2MI , GK 4-IV variant, is applied, at first twice and simultaneously with the radiation therapy and/or chemotherapy and, in the last repetition, to destroy the remaining viable cancer cells (for the schedule of the variants, see Paragraph 4.2.4). The third implementation of the GK 4-IV procedure takes account of the fact that the deterioration in the O_2 status (defense) after radiation or chemotherapy occurs after a delay of approximately 20 days.

¹ operation, chemotherapy, radiation

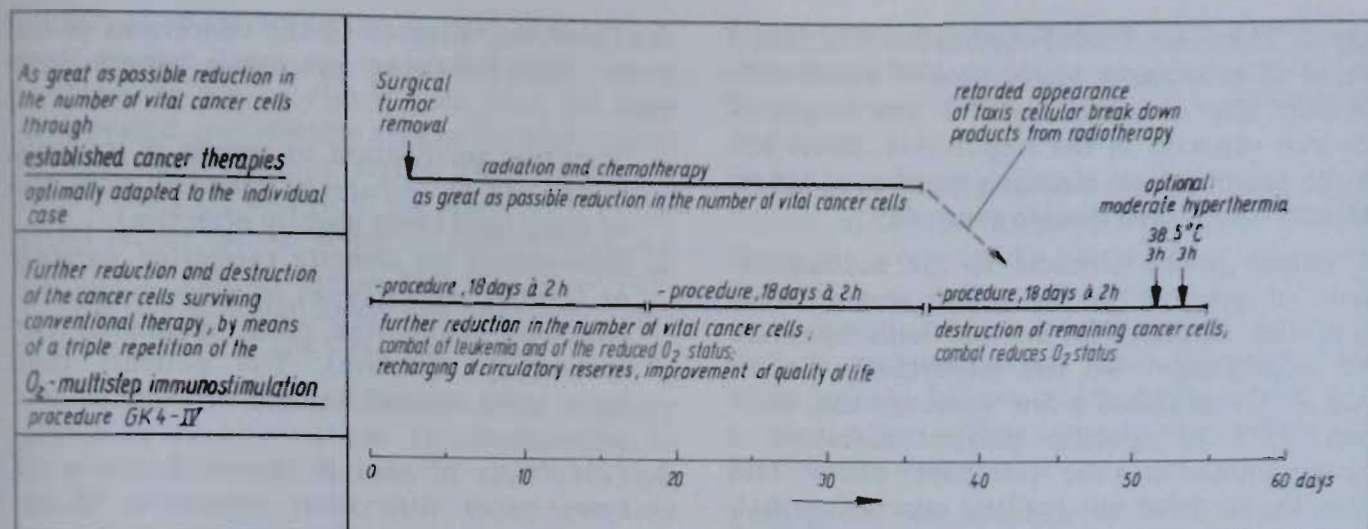


Fig. 280 Treatment programs of the highly efficient combination of conventional cancer therapies (operation, chemotherapy, radiation) with three 18-day cycles of the O_2 multistep immunostimulation (OCR- O_2 MI). Main use of the 36^h 18 day O_2 MI procedure for the destruction of the residual cancer cells which have escaped conventional therapies and for prevention of metastasis. Optional, for further increase in effectivity, $38.5^\circ C$ whole body hyperthermia, e.g. using the infrared A irradiation stretcher or by spontaneous (metabolism-conditioned) hyperthermia through hyperglycemia, can be accomplished. The improvement of circulatory reserves is so impressive that even higher doses of drugs or radiation can be envisaged

This combined treatment offers the patient all the advantages and effects that the current standard cancer therapies can offer him in his case. However, he also profits from the increased number of cancer cells destroyed by his defense system and, furthermore, from the alleviation of the side-effects of radiation and chemotherapy (increase in his quality of life in this phase) and has also, most importantly, often or with a high probability the prospect of a stop in the progression of his disease. In patients who are still sufficiently fit, the oncologist only needs to release the patient for 2 h daily for out-patient treatment at a nearby O_2 MT center during the therapy phase. The combination described should be an immediately utilizable, virtually optimal solution to the therapy problem. It results in an undeniable intensification of the effectiveness of conventional cancer therapy.

In the final repetition of O_2 MT in Fig. 280 in cases of generalized stages it should be considered whether any further methods of increasing the therapeutic efficacy should also be used (cf. Fig. 267), for example:

1. Application of the GK 4-III intensive variant with thymus or Neythymun.
2. Co-use of PIND-AVI as a further immunomodulator [343].
3. Selective over-acidification of the cancer tissue (including monitoring of the systemic electrolyte balance [214]) to intensify the chemotactic attraction of leucocytes [2]. On

the 17th and, if necessary, 18th days, increase in the blood glucose of 5–8 mg/ml for 6–8 hours.

4. Moderate hyperthermia at 38.5 – $39.0^\circ C$, using our special infrared-heated couch [462], or by induced hyperthermia.

The utilization of the concept and highly developed technology of the CMT in which the O_2 MI has been integrated for over 10 years, should also be considered for the treatment of cancer in its later stages.

The author is firmly convinced that, using the method described here, the death rate and the incidence of cancer with its great suffering could be quickly and very significantly reduced. However, since Otto Warburg's great discovery, more than 60 years ago, of the aerobic glycolysis of the cancer cells, the therapeutic usefulness of which the author, supported by Reitnauer, preached 20 years ago, cancer research has made only the smallest steps. In order to see that progress was being made it was necessary to wait for the results of double blind studies which, in the case of cancer, are often unavailable until years later. It was forgotten that creative ideas, hypotheses and even speculations can also open up new horizons. What can be done in the situation described? We, too, will need to perform many double blind studies, some with very large numbers of patients, in order to secure statistically significant results; but until such studies have been completed and acknowledged, a time-span of 30 years will have

passed. There are several reasons for this: latent period of metastases, recognition of a cure only possible after a minimum of 5 years, lack of research capacity in the responsible clinics etc. In the meantime an alarming number of cancer patients die of their disease every day.

A further severe obstacle to the accomplishment of progress in the health service arises from the *flooding of doctors with literature and information*. No less important a doctor than R. Gross stated a few years ago that more than 95% of specific medical literature is thrown unread into the wastepaper basket. This leads to the hard but realistic conclusion that, under the conditions of our time, the publication of results in medical journals is no longer enough, as was the case 50 years ago, to achieve a fast transition into practice. The firm conviction that the O₂MI and the O₂MT are of great importance for many branches of medicine *obliges* the author to ensure its fast transition into practice using non-standard methods which

are, however, adapted to the conditions of our time. The following procedure results from this:

1. Scientific publication of results in journals, books and by lectures at specialist symposia or congresses (only slightly effective).
2. *Information to directly interested patients or laymen* via all types of mass media, i.e. television, radio, the press, magazines etc. (extremely effective). The patients then force their doctors to deal with the subject in question.
3. Production of several thousand copies of every paper with what appear to be important contents. Copies sent on request (from our Institute) to patients, perhaps to be passed on to the doctors treating them.
4. Printing and sending (on request) of a *list of doctors, clinics and institutions* solidly implementing the treatments in accordance with the schedules elaborated.

5.4 Closing remarks

Looking back, we must note the *extraordinarily high number of indications for O₂MT*. Very recent individual findings point to further, probably relevant indications such as the alleviation of states of confusion and the side-effects of many drugs, increase in IQ, application during births, reduced risk in operations, acceleration of wound healing and rehabilitation, and the combat of multiple sclerosis (inhibition of attacks). For physically disabled (e.g. paralysed or amputated) persons who are subject to the long-term stress of physical inactivity, the periodic repetition of variants of the O₂MT adapted to their specific situation can be life maintaining. The large number of indications is an expression of the unique universality of the O₂MT and of the fact that O₂ deficiency (energy deficit) is the primary cause of so many illnesses and complaints.

Only clinical practice can show where, in pathogenetic chains with many members, the therapist must set other priorities than the direct combat of oxygen deficiency. Several changes, supplements and refinements of the present-day methodology will certainly be developed from practice.

It is also very striking that there are *few absolute contraindications* for this therapy, as long as the P_{O₂} increase of the inhalation air in the 2nd step is not raised above the prescribed limit

and, in the 3rd step, the possibly intended physical exertion takes account of the individual's capacity. In particular, there have not so far been any additional disorders in the regulative behavior of patients with regulatory disorders when the therapy is timed in accordance with Tables 24–33.

The research into physiology, technology and the medical application of the O₂MT, compiled in this book, resulted alongside – or, rather, from – our efforts, begun in 1963, to develop the *Cancer Multistep Therapy* (CMT). This development, which will continue to occupy us in Dresden, led in 1977 to the design of a highly selective cancer therapy, with irreversible inhibition of the blood microcirculation in the cancer tissue. Its direct target is now, after positive animal experiments and pilot studies (e.g. Fig. 82) to furnish further clinical evidence of the high therapeutic selectivity attained. Here, too, the stimulation of the metabolism of the cells and the influencing of the microcirculation form the methodological key. Here we were mainly concerned with the stimulation of the glucose metabolism, i.e. the long-term multiplication of the aerobic glycolysis of the cancer cells, which is possible in the deficiently supplied cancer tissue and leads to its strong, selective over-acidification with many therapeutically utilizable effects. Thus a

multitude of stimuli to the content of this book must be put down to our work on the cancer problem. It can be clearly seen from the facts of repeated considerable aids to the elaboration of the CMT concept arising from results of O₂MT research, and from the application of the O₂MT in the various stages of development and combat of cancer, that it was very productive to describe simultaneously the apparently very different paths of the CMT and the O₂MT.

The discovery and utilization of the capillary switching process of the blood microcirculation, which forms the basis of the O₂MT, has made it possible to *increase, long term, the energy in the human organism by approximately 15% (in healthy persons) to 80% (in weakened persons)*. This fact, which has far-reaching consequences for medicine and the

health service, was proved and evidentially documented in 1986 by spirometric measurements of the lasting rise in CO₂ production at rest.

The energy largely to re-write this book in the course of 2 months stems from two sources: from my purposeful utilization of the O₂MT procedure, and from the response to the objections and criticism made by fellow specialists such as contained in the letter from Otto Warburg, printed below, which is one of the most moving letters calling for action that have ever reached the author.

Perhaps the text of this letter written on the occasion of the 1st edition of our Cancer Multi-step Therapy book [2] can also support many a reader in his personal fight for the progress of science.

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of Cell Physiology

Berlin 33 Dahlem
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1. 4. 67

Dear Prof. von Ardenne,

I must say that I admire you when I leaf through the book. In these few years you have certainly reached the peak of cancer research; I certainly know of no single book in the whole of cancer research in which anyone else has tackled the therapy problem with the same energy and breadth. My instinct tells me that, in the long run, your victory is certain. You can only make *one* mistake now: in giving up too soon, discouraged by too much opposition. Perhaps I could be exemplary in this respect. The more opposition I found, the more I attacked and the better my weapons became.

"To dust with all enemies of Brandenburg!"

Yours sincerely

Otto Warburg